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BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

Vol. 42.] 1945. [No. 9.

SUMMARY OF RECENT ABSTRACTS.*

VII. HELMINTHIASIS.

[*Continued from* p. 614.]

Anthelmintics.

BALDWIN (p. 54) has devised a method for studying the action of anthelmintics on segments cut from the body of *Ascaris lumbricoides* of the pig. Certain substances, including santonin, act chiefly on the anterior segment, which contains the nerve ring and ganglia ; others, including hexyl resorcinol, thymol, oil of chenopodium, carbon tetrachloride and tetrachlorethylene, act on both the anterior and the intermediate segments (which are regarded as nerve-muscle preparations free from nerve ganglia).

COLLIER and ALLEN (p. 676) have found evidence that some of the soluble derivatives of phenothiazine accelerate the haemolysis of red cells which is produced by lysins such as saponin and lysolecithin. This accelerating effect may explain the haemolytic anaemia which occurs when phenothiazine is given to some species of animals.

BEATTIE *et al.* (p. 409) have successfully treated a case of acute carbon tetrachloride poisoning by the administration of methionine. The rationale of the treatment was based on the knowledge that liver damage due to chloroform anaesthesia can be prevented in this way. It is thought that the cause of liver disturbance induced by carbon tetrachloride is abnormal metabolism of methionine and related compounds.

Hookworm and Strongyloides Infection.

LOWE and LANCASTER (p. 950) report on a considerable number of men of the Australian army who returned from service in the islands of the north with hookworm infection. *Ancylostoma duodenale*, *Necator americanus* and *A. braziliense* were found, but the infections were light, and the authors concluded that such anaemia as was found was caused rather by malaria than by the hookworms. The only blood change was an increase in the absolute number of eosinophil cells. For treatment the authors used tetrachlorethylene (4 cc.), carbon tetrachloride (3 cc.), oil of chenopodium (2 cc.) or hexyl resorcinol. In

* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1944, v. 41. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

this dosage, tetrachlorethylene constantly caused muscular inco-ordination, and the authors state that the doses quoted are maximal. MAPLESTONE (p. 951) comments on the paper by LOWE and LANCASTER, to the effect that carbon tetrachloride is, and should be regarded as, a dangerous drug, a dose of 1·5 cc. having caused death on one occasion. Its toxicity is largely independent of the size of the dose, and all the evidence goes to show that it invariably causes liver damage, whether there is clinical evidence of it or not. It has been superseded by tetrachlorethylene.

KRAUSE and CRILLY (p. 139) claim that, in infection with *Necator americanus*, certain radiological appearances (called the "deficiency pattern") may be detected, which cannot be attributed to other disease. This is much more apparent in those with clinically significant infection than in those with few incidental worms; anthelmintic treatment leads to a return towards, but not to, the normal pattern in the former group. [It may be worth noting, however, that persons with clinically significant hookworm infections are usually suffering from malnutrition also.]

It has long been postulated that the anaemia of hookworm disease may be due, not only to loss of blood but also to the effect of some toxin produced by the worms. HEILIG and VISVESWAR (p. 499) remark that certain infections, and states of malnutrition, play a part in preventing the regeneration of blood, so that in these conditions even a few worms may precipitate the anaemic state, but it is unlikely that there is any worm toxin which can produce aplastic anaemia. Heilig himself, however, thinks, as a result of previous work, that the cardiac complications of hookworm anaemia are caused in part by some factor, other than anaemia, connected with the worms, and the authors have shown that perfusion of the heart of the frog with preparations of serum from patients with severe hookworm infection causes well-marked reduction in the amplitude of the heart beat. They therefore postulate a factor toxic to the heart muscle, which is not amenable to anti-anaemic treatment though its effect may be masked by the improvement caused by blood regeneration. This toxic factor is probably a toxin, not in the chemical, but in the serological sense, and the authors note that antibodies have been found in the blood of dogs infested with *A. caninum*. The existence of an anti-haemopoietic toxin has not been proved, and is improbable.

MACGREGOR (p. 949) has made a study of the bone marrow in the hypochromic anaemia found in hookworm disease. The appearances, and also those found in examination of the peripheral blood, suggest a dual deficiency of iron and (possibly) of the anti-pernicious anaemia factor, and analysis of the diets of the patients showed them to be very poor in iron, protein and in sources of the anti-pernicious-anaemia factor. A remarkable improvement takes place in patients given massive iron therapy augmented by intramuscular injections of liver extracts. This paper emphasizes the importance of dietary deficiency in the production of hookworm anaemia. THIAGARAJAH (p. 409) has found that the anaemia of women admitted to a lying-in hospital in Ceylon is of the nutritional deficiency type—hypochromic and microcytic—and this he attributes to insufficiency of iron and to damage of the intestinal mucosa by hookworms. He therefore emphasizes the need for iron therapy after disinfestation by anthelmintics.

ARANGO (p. 1053) relates the anaemia so often found in association with hookworm infestation simply to the weight of that infestation, and supports the view that it is due to continued blood loss from lesions of the intestinal mucosa. [It will be remembered, however, that other workers have laid stress on the influence of faulty nutrition, as well as of blood loss, in the production of this anaemia.] The blood picture shows hypochromic, microcytic anaemia, with reticulocytes; after administration of anthelmintics, the total red cell

count falls, but this does not happen if liver extract is given before and after their administration.

DE MEILLON and LAVOIPIERRE (p. 679) have produced creeping eruption by applying hookworm larvae (from S. African dogs, probably *A. braziliense* or *A. caninum*) to the skin. They think it unlikely that mites are the cause of similar eruptions. SMITH (p. 680) has had success in treating creeping eruption with intramuscular Fouadin, but BLANK (p. 680) reports failure by this method.

WATT (p. 766) has obtained evidence that rats infested with *Nippostrongylus muris* and placed on diets deficient in thiamin or riboflavin, were less resistant to reinfestation than controls. Plasma from normally fed infected rats has a protective action when injected into other animals, but plasma from these rats on deficient diet was not so effective.

LOWE and LANCASTER (p. 951) have treated a number of men infected in New Guinea and the neighbouring territories with *Strongyloides stercoralis*. The symptoms included chronic cough, dyspepsia and chronic diarrhoea, without anaemia but with eosinophilia. In treatment, gentian violet is disappointing, though it relieves symptoms; Fouadin, tartar emetic and emetine failed to affect the stages of the worms in the tissues.

LEVIN (p. 411) has given a general account of the clinical features of infestation with *Strongyloides stercoralis*, of which he has seen 12 cases in Russia. The severity of the symptoms may be very varied—some patients show little sign of illness, but in others the disease may be fatal, or may suggest appendicitis or peptic ulcer. Details of the symptoms are given in the original abstract. Treatment was not very satisfactory; thymol gave the best results, but gentian violet was not used. SHIKHOBALOVA and SEMENOVA (p. 411) have studied 29 cases of infestation with *Strongyloides*; they describe the prominent symptoms, and note that eosinophilia was usual. The treatment consisted of gentian violet or crystal violet given daily for 8–16 days. Symptoms showed striking improvement after this, but in some cases larvae were found to persist. Much more study of this disease is needed.

By examination of the duodenal contents, CANÇADO (p. 223) has found larvae of *Strongyloides stercoralis* in 9 per cent. of people in Bello Horizonte, Brazil. The infestation is especially prevalent among the poor.

Ascaris Infection.

FERNANDO and BALASINGHAM (p. 413) call attention to the fact that two-thirds of the population of Ceylon (of all ages) are infested with *Ascaris lumbricoides*, and that there is a case mortality rate of 8 per cent. in in-patients with *acute* ascariasis. This acute condition is not rare, especially in children under 5; it is postulated that an infestation may give rise to acute symptoms because of toxic effects of products liberated when the worms die in the intestine. So many persons are infested but do not present the acute syndrome that some other factor than infestation seems to be concerned, and injection of *Ascaris* material can cause the symptoms of acute ascariasis. The manifestations may be:—acute inflammation of the alimentary tract (like infective diarrhoea); toxic and cerebral, sometimes simulating meningitis; acute abdominal symptoms, of partial obstruction or simulating appendicitis; respiratory symptoms due to larval infiltration of the lungs; or mixed symptoms. Treatment for these forms is outlined, but for the details the original abstract should be consulted.

ARDAO and ZERBONI (p. 767) point out that faecal examination may be negative for the eggs of *Ascaris lumbricoides* if the worms are all males or infertile females. A diagnosis may be made radiologically, though a negative finding does not necessarily exclude ascariasis. The authors give an account of

the radiological appearances which may be seen after the ingestion of an opaque meal in *Ascaris* infection.

EARLE (p. 768) reports a case of asthma apparently due to infection with *Ascaris*.

BAUMANN (p. 859) records the case of a man with acute pulmonary symptoms, pleural effusion and eosinophilia, who shortly afterwards began to pass eggs of *Ascaris* in his faeces. The author thinks that the syndrome was probably due to the larvae of the worm, in the pulmonary stage of their development, and, in this connexion, discusses Löffler's syndrome. SOMMER (p. 680) expresses the view that Löffler's syndrome of pulmonary infiltration and eosinophilia may be allergic in nature and that the allergic state may be due to infestation with *Ascaris*. The pulmonary lesion may be due to larvae of the worm in a sensitive person, and the author, in fact, proposes the name eosinophil anaphylactic pneumonia for this condition. He quotes cases in support of his view, especially one in which the symptoms cleared up quickly after expulsion of a single male worm, and in which the allergic state to *Ascaris* antigen was very marked, so much so that intradermal injection of the antigen led to typical anaphylactic shock.

BRUNNER *et al.* (p. 952) have investigated the subject of skin sensitivity to antigens prepared from *Ascaris*, in dogs infested with various intestinal nematodes. For details, the reader should consult the original abstract.

LONGINOV (p. 140) reports favourably on the use of hexylresorcinol in infestations with *Ascaris lumbricoides*. TRIM (p. 596) has studied the action of hexylresorcinol on *Ascaris lumbricoides*, and finds that the main path of entry into the tissues of the worm is through the cuticle. Results of a study of the uptake of the drug by the worm in the presence of biological substances such as are found in the alimentary tract are given in the original abstract. Bile salts tend to inhibit the uptake, but may have a different effect *in vivo* because of the interference of other components of the complicated emulsion in the small intestine, and because the drug is adsorbed to mucin.

OLIVER-GONZÁLEZ (p. 223) has studied the action, on larvae of *Ascaris lumbricoides* of the pig, of antibodies in the sera of rabbits infected with *Ascaris* eggs, or injected with extracts of the whole adult worms. These antibodies cause the formation of precipitates round the orifices and cuticle of the larvae, and also immobilize and kill a large proportion of them. Extracts of isolated tissues of *Ascaris* did not provoke the formation of such potent antibodies.

OLDHAM and WHITE (p. 769) have shown in pigs that the condition known as "white spot liver" can be produced by feeding the animals with embryonated eggs of *Ascaris lumbricoides*. The distribution of the lesions in the liver indicates that infection is conveyed by the portal vein, and not by way of the peritoneal cavity.

Filariasis.

In the *Bulletin of the U.S. Army Medical Department* (p. 860) there was published an account of filariasis in troops in the Pacific Islands. It is noted that the earliest onset of symptoms occurred 3 months after arrival, and consisted of lymphangitis, swelling of the glands or acute inflammation of the scrotum, testis and spermatic cord. No microfilariae were seen in the blood, but adult worms were found in some biopsy material. Intradermal tests were positive in the majority of the patients, but were also positive in a few controls. It is evident that signs and symptoms can develop very soon after exposure to infected mosquitoes.

DICKSON *et al.* (p. 303) have investigated filariasis in the natives of the Samoan islands, and in American soldiers there. Infection is present in a high proportion of the islanders, and a considerable number of Americans have been infected.

Failure to find microfilariae in the blood does not exclude the condition. Acute lymphadenitis or lymphangitis may be the earliest sign of filariasis, usually in the arm or leg; but there is a highly characteristic scrotal lesion with funiculitis. There is a tendency to multiple involvement and recurrence, but there are no severe constitutional symptoms. Skin tests with an antigen prepared from *Dirofilaria immitis* were positive in the large majority of patients tested. The authors think that there is not much chance of recurrence in patients repatriated to the United States, and that the disease should not prove a serious disability. Treatment consists of rest and reassurance—drug therapy has so far failed.

Burhans *et al.* (p. 599) give a detailed list of the symptoms and signs found in men of the Unites States Navy who had returned from the South Pacific diagnosed as suffering from lymphangitis. Though no parasites were found, the men were thought to be suffering from filariasis, and nearly all had lymphatic gland involvement. Details should be sought in the original abstract. Sulphonamides were not useful in treatment, but X-ray therapy promptly brought about decrease in the size of the glands; it is not yet known if this is a permanent effect.

Neumann (p. 954) describes filariasis as it affects white persons in the Samoan Islands. Symptoms may be absent, even with heavy infection, or they may be allergic (with oedema), or due to streptococcal infection (with fever and lymphangitis) or to staphylococcal infection (with local pain or abscess). Repeated attacks of streptococcal infection lead to elephantiasis; this infection is amenable to sulphonamide treatment, whereas the staphylococcal infections are not. Microfilariae are not found in the blood in the early stages of filariasis, and diagnosis must rest on the clinical symptoms. After leaving the endemic areas, white men are usually free from these attacks.

Michael (p. 956) makes the point that, in several thousand blood examinations on men of the United States forces, infected with *Wuchereria bancrofti* in the Samoan region, he failed to find microfilariae. Most of the men developed symptoms 7–9 months after exposure to infection, and most had lymphangitis and funiculitis. Skin tests with an antigen prepared from *Dirofilaria immitis* were positive in 87 per cent. In 36 of 120 specimens removed at biopsy, living or dead adult worms were found; these were in the peripheral lymphatics or lymph nodes. It seems that spontaneous recovery takes place after the patient leaves the endemic area. Flynn (p. 956) reports similar findings.

Lowman (p. 600) has found microfilariae of *W. bancrofti* in the blood of an infant aged 14 months in a South Pacific island, and argues that the early appearance of filariasis in American troops in that area is possible, and that this should be borne in mind by medical officers.

Clearkin (p. 598) notes that the absence of microfilariae from the blood is not evidence of the absence of filariasis, and that a positive Fairley skin test may be accepted as confirmation of diagnosis. Pathological changes may be the result of blockage of lymphatics, infection or allergic reactions; for the latter the author is experimenting with desensitization methods, using extracts of *Dirofilaria immitis*. This treatment promises to be useful. Streptococcal vaccines have also been used with some success.

Hartz (p. 955) gives a detailed description of the histological appearances in the granulomata found in the lymphangitic lesions of filariasis. Details should be sought in the original abstract, but a mistake in the abstract should be corrected. It is stated that there is no necrosis, and little eosinophilia, if the *microfilariae* are alive, but that large numbers of eosinophils may be present if the *microfilariae* have been dead for some time. In each case the author, in the original, used the word *macrofilariae*, and the statements refer, as would be expected from the context, to the adult worms.

Reports on the after-histories of patients who have undergone amputation of a limb for elephantiasis are scarce. RAO (p. 59) describes a patient whose leg was removed for elephantiasis and recurrent lymphangitis, but the condition appeared in the other leg and in the stump. The amputation, therefore, conferred no benefit beyond the removal of elephantoid tissue.

BOZICEVICH and HUTTER (p. 1055) have used an extract of *Dirofilaria immitis* as antigen in skin tests for infection with *W. bancrofti*. All the subjects tested, who had been exposed to infection, gave positive results to the intradermal test at a dilution of 1 in 8,000, but some of these were positive to other antigens at the same dilutions. Complement fixation tests were not found to be useful. The authors conclude that the antigen, in a dilution of 1 in 8,000, may be useful in the diagnosis of filariasis, provided that it is used with controls of canine serum and *Trichinella* antigen, in the same dilution ; stronger solutions are less specific. The reactions produced may be immediate or delayed ; the latter occur only in persons who give the immediate reaction.

CULBERTSON and ROSE (p. 772) have achieved some apparently favourable results, in the treatment of cotton rats infected with the filaria *Litomosoides carinii*, by the use of stibamine glucoside (Neostam) in relatively large doses. They suggest that this drug may be useful in human filariasis.

CULBERTSON *et al.* (p. 770) report work on an antigen from *Litomosoides carinii* of the cotton rat, which they used for intradermal tests in persons infected with *Loa* and *Onchocerca*. These appear to be favourable, but more work is to be done on possible cross reactions. The same authors (p. 771) used antigens from this worm in skin tests, precipitin and complement fixation tests, in a group of United States soldiers suffering from lymphadenitis and other signs of suspected filariasis. The tests gave 81–75 per cent. of positive results, but the correlation between them was only fair. It is probable that a significant proportion of persons not infected with filariae give positive results to these tests, and there may be difficulty in relation to infestations with *Trichinella*, *Ascaris*, *Trichuris* and hookworms.

MENON *et al.* (p. 770) have studied the development of the filaria of the lizard, which resembles *Wuchereria bancrofti*, and discuss their findings in relation to the latter.

SCOTT (p. 683) describes what he believes to be the first case of onchocerciasis in a Gambian. *O. volvulus* embryos were found in the anterior chamber of the eye, and in the skin. In a second case there was oedema of the eyelid, ciliary flush and optic neuritis, but no microfilariae could be found in the eye, though they are present in the skin. The author considers the possible causes of such a syndrome, and concludes that the most likely explanation is the existence of anaphylaxis to the toxins of *O. volvulus*. NETTEL (p. 305) discusses the routes of invasion of the eye in onchocerciasis, and gives a classification of the lesions found throughout the body in an area of high endemicity in Mexico. Details should be sought in the original abstract.

LOEWENTHAL (p. 305) produces evidence to show that the papular dermatosis which may accompany onchocerciasis is not, as has been thought, due to the bites of *Simulium damnosum*. It is more likely that the skin is sensitized to the proteins of the larvae of the worms, and that the itching is due to this.

MAZZOTTI and OSORIO (p. 957) have experimented with two antigens prepared from *Onchocerca caecutiens* injected intradermally, in onchocerciasis. Positive results are given in most diagnosed cases, but there is a high proportion of false positives given by uninfected persons. The test, therefore, does not seem to be useful in diagnosis. WRIGHT and MURDOCK (p. 1054) have used an antigen prepared from *Dirofilaria immitis* in an intradermal test for onchocerciasis. All the subjects in whom *Onchocerca* embryos were found were positive to this test, but many of the controls (who were infected with other nematodes) also

gave positive reactions, and the authors conclude that care is needed in the evaluation of intradermal tests.

Enterobius Infection.

YOUNG (p. 141) found that 42 and 55 per cent. of two groups of London children were positive for eggs of *Enterobius* on examination (repeated twice or thrice) by the "Cellophane" swab technique. In the first group, only 5 per cent. showed eggs in the stools. DONALDSON (p. 141) reports infestation with *Enterobius* in 46 and 31 per cent. of boys and girls in an institution in Ohio, in which the living conditions were good.

JONES and HOLLAENDER (p. 596) show that radiations which are quite intense in sunlight are lethal to the eggs of *E. vermicularis* and *A. lumbricoides*. Sunlight itself is probably more lethal than the radiation produced by a mercury lamp, especially if correlated with high temperature and low humidity.

Trichiniasis.

In a description of an outbreak of trichiniasis near Montevideo, CLAVEAUX *et al.* (p. 501) make special note of a common condition in which there were transitory pulmonary symptoms and eosinophilia, resembling Löffler's syndrome; the authors therefore suggest that such findings should indicate a search for *Trichinella*. Similarly, they think that in a patient with positive Wassermann or Kahn test, but without history of syphilis, trichiniasis should be suspected.

On the supposition that the toxic effects of infestation with *Trichinella* may be due to release of histamine through tissue destruction, HAMANN (p. 415) estimated the histamine content of blood and of various organs of satisfactorily infected guineapigs and rats. The results indicated some increase, apparently due to the infection, as against the values found in controls, in the blood and in inflamed duodenal tissues, but not in liver, kidneys and skeletal muscles. There was no consistent correlation between blood histamine and eosinophilia. The results, however, were difficult to evaluate because there was great variability in both the experimental animals and the controls.

CARRICK (p. 685) has investigated the effect of infestation with *Trichinella*, in animals, on the activity of the parathyroid glands. Details should be sought in the original abstract.

MAZZOTTI and PASTRANA (p. 958) have found that calcified cysts of *Trichinella spiralis* tend to become disintegrated during the process of digestion with artificial gastric juice. This probably explains why the numbers of cysts revealed by this process is often smaller than the number found by the compressorium technique.

WRIGHT and OLIVER-GONZÁLEZ (p. 225) have examined by electrophoretic methods the sera of rabbits infested with *Trichinella spiralis*, and have found an increase in gamma globulin. Antibodies against both larvae and adults were present in the gamma globulin. The authors recall that anti-adult substances in serum protect, to some extent, against the intestinal stage of infestation, but that the antilarval substances give no protection against intestinal infestation.

As a result of infestation of guineapigs with larvae of *Trichinella*, of one sex only (so that there can be no multiplication), ROTH (p. 59) has shown that a considerable degree of immunity against subsequent infestation by larvae of both sexes (as in natural infection) is induced. This immunity is therefore conferred by the intestinal phase of *Trichinella*, and is apparently a true acquired immunity. It would probably be much more effective if larvae were present in blood and muscle of the host animal.

MELCHER (p. 225) has investigated the antigenic power of six chemical fractions obtained from larvae of *Trichinella spiralis*. Of these, the polysaccharide and the acid-soluble protein are the potent precipitating antigens, and skin reactions are given with the acid-soluble protein, and an alkaline extract which itself is an earlier stage of the acid-soluble fraction. The results indicate that the acid soluble protein is the fraction which other workers, using a less refined technique, have regarded as valuable for the diagnosis of trichiniasis. There is no evidence of an antigen common to *Trichinella* larvae and adult *Ascaris*, as has been claimed by other workers.

Some German medical officers have thought that treatment of trichiniasis with Fouadin leads to improvement in the general condition, though others are sceptical. SCHREIBER (p. 686) has failed to find any influence of Fouadin and other antimonials in affecting the infestation of animals with *Trichinella*.

Syngamus Infection.

FONT (p. 302) draws attention to three patients from whom *Syngamus laryngeus* (male and female together in copula) were removed from the oesophagus or larynx. These slender worms, which may be mistaken for dilated capillaries, cause constant irritation, with violent coughing ; removal cures the condition. *Charles Wilcocks.*

RABIES.

A REVIEW OF RECENT ARTICLES. XLIII.*

i. *Virus.*

JONESCU[1] states that he has failed to find in the literature any reference to studies on the autolysis of rabies-infected brain. He has therefore placed on record some observations on the subject. Within limits, autolysis proceeds more rapidly, the higher the temperature. The conservation of the tissue at very low temperatures and the associated prolonged survival of the virus is not due alone to the arrest or diminution of bacterial multiplication, but also to the hindrance to the normal autolytic process. At 10°C. the advance of autolysis is difficult and at 18°C. relatively slow, but it is favoured by raising the temperature to 37°C. At 50°C. autolysis is stopped completely.

The author has made observations at 18°C. and 37°C. The brains of a rabies-infected dog (street virus) and a " normal " or uninfected dog were removed aseptically and kept at 18°C. in separate glass containers under conditions in which bacterial contamination was excluded. The rabies-infected brain resisted autolysis for a longer time than the brain of the normal dog. After eight days the virus-infected brain appeared unaltered whereas the normal brain was flattened and there was a reddish exudate, and this difference is attributed by the author to the inhibition of the normal autolytic enzymes by the virus.

Fragments were removed at intervals from various parts, including the centre of the virus-infected brain, and these were emulsified and inoculated intracerebrally into rabbits in doses of 0·2 cc. After three months this brain was " completely autolysed " and it had assumed the appearance of a whitish paste. On microscopic examination the cells were found to be " completely killed "

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* For the forty-second of this series see this *Bulletin*, 1945, v. 42, p. 165.

[1] JONESCU, D. Untersuchungen über die Autolyse von Tollwutgehirnen. *Zent. f. Bakt.* I. Abt. Orig. 1943, Dec. 11, v. 151, No. 1, 21–5, 1 fig. [15 refs.]

and rabbits could no longer be infected by intracerebral inoculations with suspensions of the brain, but Negri bodies could be seen fairly well stained by the Lentz method.

In another experiment a reinforced virus " J " was used, with an incubation period of three days, and the presence of virus in the autolysed brain was demonstrated after four months by the inoculation of rabbits intracerebrally. The incubation period in these was prolonged to six days. After four and a half months the virus was inactive. In a third experiment at 18°C. in which the " Babes " fixed virus was used, active virus was demonstrable in the autolysed brain after three months.

Advantage was then taken of the increased rate of autolysis at 37°C. to make more detailed observations than were possible at 18°C. After 24 hours at the higher temperature there were already macroscopic changes detectable in the rabies brains. There was a rose-coloured exudate which later became dark brown. After three days' autolysis at 37°C. a fragment from the brain was easily emulsified, and after five days whitish formations appeared on the surface of the dark-coloured brain which had spread out on the bottom of the container. These " efflorescences " seemed to consist of crystals.

In an experiment at 37°C. in which a rabbit fixed virus was employed, observations were made on an autolysed rabies brain (rabbit) and an autolysed normal rabbit brain. In a period covering 15 days the pH of both brains altered from 7·6 to 7. Virus was detectable by the inoculation of white mice after nine days but not after 11 days or longer. Similar results were obtained in experiments with the brains of a dog and two cattle, infected with a street strain of virus. Microscopic studies were made on the autolysed brains of rabbits and dogs infected with fixed strains of rabies virus, and on the autolysed brains of a dog and cattle infected with a street strain. After periods of 2, 4, 6, 8, 10 and 13 days at 37°C., portions of the Ammon's horn of these brains were removed and fixed in acetone, embedded in paraffin and sections were stained by the Lentz method.

After three days' autolysis, fine oxyphilic granules were observed in the Ammon's horn of the brains of the animals infected with the fixed strains of virus ; some were like small Negri bodies and they were not found in the autolysed brain of a normal animal.

The microscopic findings in the sections of the Ammon's horn of the autolysed brains of the animals infected with street virus were as follows :—After one day at 37°C., the cytoplasm of the cells had disappeared ; the nuclei showed first pyknosis, then achromatosis and finally chromatolysis. Whereas the nuclei, after 10 days, had completely disappeared, the Negri bodies, " especially the mature forms with internal structure as well as the morula forms or forms with basophilic inclusions," maintained their characteristic appearances and were distinctly oxyphilic. Up to the ninth day, virus could still be demonstrated in the autolysed rabies brains by the inoculation of rabbits by the intracerebral route. After that time, although Negri bodies were still present, active virus could not be detected. The Negri bodies in the autolysed brains appeared to be double the size of those seen in the non-autolysed tissue. [The certainty with which it can be determined that the brain tissue is infective or non-infective is controlled by the limitations of the sensitivity of the test employed to decide this. Any attempt to correlate virus infectivity with the presence or absence of oxyphil granules or Negri bodies must be considered as purely speculative. It might be interesting to consider these observations in relation to the theory of Remlinger and Bailly on the attenuation of the virus of rabies during the preparation of vaccine by the Pasteur method (see this *Bulletin*, 1943, v. 40, 195 ; 1944, v. 41, 904).]

ii. *Symptoms and Diagnosis.*

BREAULT[2] refers to a human case of rabies which occurred during a localized outbreak in the summer and autumn months of 1944 in which many dogs and cats and a cow contracted the disease. The case is chiefly of interest because of the history, and the dog which bit the boy did not appear to be rabid or " wild." It bit the boy in the leg on provocation, and disappeared. The wound was deep and lacerated and was stitched. The stitches were removed one week later and the wound healed normally. The boy was well for seven weeks. On August 22 he complained of " crampy " pains in the leg, and was feverish. On August 25, because he still had fever and had backaches and stiffness of the dorsal muscles he was sent to hospital, as poliomyelitis was suspected. He was, however, sent home the same day as this disease was ruled out. Three days later he had delirium and hydrophobia, and he was readmitted to hospital on August 29. There was unbearable itching of the leg which had been bitten. The boy died four days later and Negri bodies were demonstrated in sections of the hippocampus and cerebellum removed at autopsy.

HERZOG[3] states that he " found independently in 1941 " a method for the diagnosis of rabies which had been " described by VAN GEHUCHTEN and NELIS in 1900 but had been completely forgotten after the discovery of Negri bodies." [Observations on the limitations of the method were made by the reviewer when discussing a previous paper by the author on the same subject (this *Bulletin*, 1943, v. 40, 199) ; it was indicated that the observations of van Gehuchten and Nelis had not been completely forgotten. As already pointed out, the presence of nerve ganglionic lesions may be said to provide strong presumptive evidence of rabies if the history suggests it, and this should be confirmed by inoculation of animals if possible with such suitable material as may be available. It was realized early that even greater prudence would have to be exercised in interpreting negative findings in the histological examinations of nerve ganglia from suspected cases (in a book published in 1903, the year Negri bodies were first described, *viz.*, " Les Maladies Microbiennes des Animaux " by NOCARD and LECLAINCHE, v. 2, p. 453–5, reference is made to the lesions first described by van Gehuchten and Nelis).]

In the present paper the author reports that of 75 subjects (7 human beings and 68 animals) suspected of having rabies, 52 were found to have the disease.

A comparison was made of different methods of diagnosis by microscopic examination of nervous tissue, such as examination for Negri bodies in the Ammon's horn, histological examination of the *ganglion nodosum* of the vagus nerve, the superior cervical sympathetic ganglion or the mesencephalon and the medulla. [Incidentally, in the literature on rabies one sees quite often a statement to the effect that no Negri bodies were found in the *Cornu Ammonis*, but the fact should not be forgotten that although Negri bodies are often found in the hippocampus, even when the disease is fully developed they may be absent from this site and from the cerebellum, but may be found in other parts of the brain in so-called " predilection " sites (see for example, this *Bulletin*, 1935, v. 32, 173 and 174 for observations by MURATOWA, THOMAS and JACKSON, and NICOLAU and KOPCIOWSKA).] In " almost 50 per cent." of Herzog's 52 " cases of rabies " he could not find Negri bodies in sections of the *Cornu Ammonis* stained by the Lentz method. However, simultaneous histological examination of the *ganglion nodosum* from the same cases always disclosed the

[2]BREAULT, H. J. Hydrophobia. *Canadian J. Comp. Med.* Gardenvale, Quebec. 1945, Apr., v. 9, No. 4, 110–13.

[3]HERZOG, E. Histologic Diagnosis of Rabies. *Arch. Pathology.* 1945, Apr., v. 39, No. 4, 279–80, 2 figs.

alterations described by van Gehuchten and Nelis in 1900, and again described by the present author. It is suggested that if examination of the Ammon's Horn and *ganglion nodosum* yields negative results, the lesions of a " rabies encephalitis " may be sought in the mesencephalon and medulla. The author states that if the results of such examinations are all negative it is not worth while to inoculate test animals, as the bitten person may be considered free from rabies and spared vaccination, " but in doubtful cases white mice should be inoculated and a result will be yielded in 15 days."

iii. *Pathology.*

Jonescu[4] refers to three cases of " natural " immunity, two in dogs and one in a male goat. He previously recorded two similar cases in dogs (this *Bulletin*, 1935, v. 32, 609 ; 1936, v. 33, p. 747.).

He points out that individual differences in susceptibility to various infective agents are exhibited by animals which can be infected with these agents. In the case of rabies there are known to be species refractory to infection, cold-blooded animals, snakes and fish ; partially refractory species such as hibernating animals, and susceptible species such as dogs, cats, rabbits, etc. In rare cases certain animals belonging to the susceptible group may exhibit a high spontaneous degree of resistance to inoculation with virus, but this resistance can often be broken down on reinoculation by more massive doses of virus, especially by the intracerebral route. In one of the two previously recorded instances, the dog, after resisting an intraocular inoculation of a reinforced virus strain J, received in succession nine intracerebral inoculations of 1 cc. of a 1 : 50 dilution of a fixed strain of virus. The author concluded that the dog had a natural immunity.

The cases recorded here were in " domestic " sheep, dogs and a goat.

Case 1 :—In December, 1940, nine dogs were inoculated with 0·5 cc. of a 1 : 20 suspension of a fixed strain (dog) of virus, intracerebrally. One 3-year-old sheep-dog withstood the inoculation. In January, along with four other dogs, it received a second intracerebral inoculation of 1 cc. of a similar suspension. It resisted this, whereas the four other dogs did not. However, the dog succumbed to a third inoculation made in January, 1943, and its brain proved infective for a rabbit by intracerebral inoculation. The period of paralysis was more prolonged in the resistant as compared with the control dog, eight days instead of two days.

Case 2 :—On August 21, 1941, 20 dogs were inoculated intracerebrally with 0·5 cc. of a 1 : 20 suspension of fixed virus ; 19 developed the disease on the seventh day, but one three-year old sheep-dog resisted. It received a second intracerebral inoculation of 1 cc. of a similar suspension on August 30, 1941, along with 15 other dogs. It resisted, whereas the 15 dogs developed paralysis on the seventh day. No symptoms developed after a third intracerebral inoculation of 1 cc. of a 1 : 10 suspension of fixed virus on May 17, 1943, whereas four control dogs showed paralysis on the seventh day. The dog succumbed, however, to a fourth intracerebral inoculation on June 24, 1943. The paralysis lasted 13 days as against the usual two days. Two rabbits, inoculated intracerebrally with a suspension of its brain, remained healthy, suggesting that " autosterilization " had occurred.

The history of the goat is somewhat similar. It resisted three intracerebral inoculations with fixed virus, but finally developed paresis which lasted 58 days after the last inoculation, and it died, and virus was recovered from its brain by inoculation of rabbits intracerebrally. Studies were made of blood samples

[4] Jonescu, D. Untersuchungen über die natürliche Immunität bei der Tollwut. *Zent. f. Bakt.* I. Abt. Orig. 1944, May 10, v. 151, No. 4/5, 254–60. [18 refs.]

collected from the two dogs five days after each inoculation. An increase in the number of eosinophils in the blood was observed up to and after the time when the fatal inoculations were given. The author has restated his opinion, expressed in 1935 [reference above], that the eosinophilia can be used as an indication of the degree of immunity, and suggests further that it might be used as a guide to the issue in following the course of vaccine treatment. He also describes experiments *in vivo* and *in vitro* in support of his contention that the leucocytes probably played a considerable part in the destruction of the virus introduced, and the resistance of the animals under discussion, but his results and conclusions are not entirely convincing. He could not demonstrate that the blood serum collected from either of the dogs at different times during the course of the experiments had any neutralizing action on the virus [the tests were not made in such a way (*i.e.*, not on a quantitative basis) that much reliance could be placed on the author's negative findings]. The author believes that other factors, such as a basic hereditary resistance, cannot be excluded from the discussion of such observed cases of exceptional resistance to infection [there are of course other possibilities in a country in which the disease is endemic, for instance: 1, a previous light infection of the animal by a peripheral route, such as might result from a bite; 2, intra-uterine infection with virus, with a non-fatal issue at birth; 3, congenital as distinct from hereditary immunity].

iv. *Methods of Treatment and Statistics.*

Durieux[5] reports that the strain of fixed virus used for vaccine production at Dakar is the Tangiers strain sent in 1922 and, at the time of writing, it had been passaged 416 times at Dakar and 944 times since its receipt at Tangiers. The incubation period in rabbits inoculated intracerebrally is 5 to 6 days. A carbolized vaccine of the Fermi type is employed and sheep are inoculated with the rabbit virus for its preparation, but the strain is never passaged from sheep to sheep [incidentally, it is understood that owing to the shortage of rabbits, sheep are now used also at the Pasteur Institute, Paris, for vaccine production]. A 5 per cent. suspension of nervous substance is used and carbolic acid is added to produce a concentration of 1 per cent. The vaccine is distributed in 6 cc. amounts in ampoules and two bacterial sterility tests are carried out anaerobically and aerobically, the first when the brain is removed from the sheep and the second when the vaccine is put into the ampoules. The vaccine for use at the central institute is placed at 25°C. for 24 hours and then stored at 5°C. If the vaccine is for use elsewhere in the service, it has to be transported by aeroplane, and is therefore not first placed at 25°C. before despatch; it is placed in cold store on arrival at the subsidiary centre. If sent out again it is kept in ice during transit. The vaccine is considered to be usable up to four months after preparation if used at the central institute, and up to two-and-a-half months if distributed to sub-stations, or centres of medical assistance. During 1941 and 1942, 409 patients were treated in the whole territory of the A.O.F., and no deaths and no paralytic or other accidents were recorded.

v. *Rabies in Animals.*

Hudson[6] reports that rabies has been known for a long time to the native inhabitants of the South Kavirondo province of Kenya. They call the disease

[5] Afrique Occidentale Française: Rapport sur le Fonctionnement Technique de l'Institut Pasteur en 1942 [Durieux, C.] pp. 41–8. Service de la râge.

[6] Hudson, J. R. A Short Note on the History of Rabies in Kenya. *East African Med. J.* 1944, Nov., v. 21, No. 11, 322–7. [10 refs.]

in dogs and jackals, " swao." The author believes that the disease must have occurred in the colony before the advent of Europeans. STORDY in 1909, however, stated in the Annual Rept. of the Veterinary Department, that no case of rabies had been recorded in East Africa and this statement appeared again in the 1912–13 report. The earliest case to be recorded occurred near Nairobi in October, 1912 and was that of a dog which had been attacked and bitten by a jackal. Negri bodies were found in its brain and confirmation of the diagnosis was obtained by experimental animal inoculations. Further cases, all with the same history, followed rapidly in the Nairobi and Kiambu areas. Jackals were reported to have lost their fear of man and to have attacked natives without provocation. The outbreak lasted till 1916. Rabbits were infected by inoculation with material collected from the infected animals.

The first human case appears to be that recorded by GREEN in 1928 [this *Bulletin*, 1928, v. 25, 709]. A native woman living in Central Kavirondo died from rabies a month after having been bitten by a dog. It has been stated that the disease was more or less enzootic in the North Frontier Provinces between 1912 and 1929. The next case reported was in 1931, and the disease persisted in certain parts until 1936 and in others to 1938. A new wave of rabies started in 1944. The disease appears to be conveyed in the forest areas and has not spread down into the Rift Valley. Rabies in East Africa appears to be spread by jackal and dogs and there is no evidence to date of *Viverridae* playing any part, as in South Africa.

It has been found that jackals which attack human beings or enter houses or compounds are infected with rabies on examination. The " dumb " or paralytic form is probably more frequent than the " furious " type. In the majority of cases the disease could be transmitted to mice and rabbits by intracerebral inoculation, and Negri bodies could be demonstrated. In four cases out of the total of 167 recorded, Negri bodies could not be demonstrated in the hippocampus of the infected animals and the diagnosis was confirmed by passage to rabbits and mice.

Apparently the natives know rabies as a disease of dogs and do not attach any importance to the bite of the infected animals. Human cases are attributed to witchcraft or the casting of spells. A similar position exists in French African Territory where the natives call the disease in dogs " oulou fato." [It seems that the Kenya strains of rabies virus are not like the " oulou fato " strain studied by NICOLAU, MATHIS and CONSTANTINESCO (this *Bulletin*, 1934, v. 31, 145), associated with " blue Negri bodies "—staining blue with Mann's double stain.]

vi. *Miscellaneous.*

REMLINGER[7] stresses again the necessity of a Second International Conference on Rabies. He now suggests that the meeting place should be in Europe and proposes Spain as a likely spot, with many points to recommend it. He urges that the representatives of the different countries should be those actually engaged in the study of the disease and that informality should characterize the discussions. The author tentatively sets out a number of matters which require urgent attention. The list is roughly as follows, with certain trimmings by the reviewer: (1) The advisability and practicability of standardizing rabies vaccines, giving due consideration to the strain of virus to be used, the method of preparation, and the technique and standard to be aimed at in estimating potency. (2) Discussion of new information on immunological and immunogenic differences between strains of the virus of rabies, and of the factors which may

[7] REMLINGER, P. Sur la nécessité d'une nouvelle conférence internationale de la râge. *Arch. Inst. Pasteur. d'Algérie.* 1944, June, v. 22, No. 2, 141–4.

affect the characteristics of a strain. (3) Discussion of the possibility of vaccinating domestic animals, including dogs, cats, horses, sheep, cattle, goats and pigs, and of the arguments for and against the general application of such a policy in countries in which the disease is endemic. (4) Consideration of the experimental animals of choice for different purposes, diagnosis, determining virus potency, the antigenic potency of vaccines—mouse, rabbit, guineapig, dog, monkey?

Rabies is a world-wide problem and there should be the maximum exchange of information on the disease and on the methods employed in the different countries to combat and control it. Some countries are more favourably placed geographically than others, and in them it is easier to prevent the introduction of the disease and to limit its spread and the possibility of its becoming endemic, should the regulations in force break down. The British Isles among other countries is so placed, but while such a country may be regarded with envy by its less fortunate neighbours, that is no reason why its endeavours should not be fully comprehended and, if at all possible, imitated to some degree. Co-operation is necessary between nations in stamping out or limiting the ravages of such a dread disease. In the same way our own Dominions and Colonies from which danger may spring, should have knowledge of the possible loopholes in the system of control. Recently attention has been drawn in a *Monthly Bulletin*[8] published under the aegis of the Medical Research Council, and in an Annotation in the *Lancet*[9], to the risk of the reintroduction of rabies into Great Britain if due attention is not paid to the regulations which are in force. In view of this risk it is imperative that everyone should have full knowledge of the possible effects of criminal negligence in evading the regulations. As FIFE[10] has pointed out in describing a case of rabies in man, many people (and this includes medical and veterinary officers in Great Britain, where, outside quarantine kennels, no case of rabies has been confirmed since 1922) have forgotten the serious nature of the disease and are not fully aware of the means by which the country has been kept free of it. [It may be recorded here that, from information received from the Ministry of Agriculture, there were 2,557 cases of rabies in animals from the year 1887 to 1898, a period of 11 years. Regulations, which since 1897 have gradually made more stringent the restrictions on the importation of canine and feline animals, have produced a most satisfactory result. There were 46 cases between 1897 and 1902 (six years), but between 1903 and 1917 there were none. During the latter half of the 19th century the annual human deaths from hydrophobia increased to the alarming total of 79 in 1877. Since 1898 only two deaths from hydrophobia have been recorded. The regulations in force require all canines and felines landed in Great Britain from abroad to be quarantined, for a period of six calendar months after landing, on premises approved by the Ministry of Agriculture. Now some may imagine that such a rule is over-cautious, and perhaps unnecessary. In order to stifle such an objection it should be pointed out that, from information received from the Ministry of Agriculture, there have been no less than 16 cases of rabies in quarantined dogs from 1919 to 1939, a period of 21 years. In six of these cases the disease developed from 1 to 12 days after the dog was landed in this country, in five the disease developed between 1 month and $3\frac{1}{2}$ months after the dog was landed, and in four cases, between 4 and $5\frac{3}{4}$ months. In the 16th case the period of quarantine was up on November 1st, 1929, and the dog was kept in isolation for a further period at the

[8]MONTHLY BULL. MINISTRY OF HEALTH & EMERGENCY PUB. HEALTH LAB. SERVICE (DIRECTED BY MED. RES. COUNCIL). 1944, Dec., v. 3, 220–22. Rabies.

[9]LANCET. 1944, Nov. 11, 628–9. The Menace of Rabies.

[10]FIFE, J. G. Case of Rabies in Man. *Lancet.* 1945, Jan. 13, 53–4.

owner's request ; it developed rabies 6 months and 24 days after arriving in Britain.

The experience of the Ministry of Agriculture has therefore fully justified the six months' quarantine period. The period of six months' quarantine is based upon the period of incubation of rabies, which may be longer even than six months, but the cases in which the incubation period exceeds six months are very exceptional. It is not considered practicable to legislate for these exceptional cases, but of course it is realized that there is still a risk, as the above records show ; there are, however, other regulations for dealing with rabies in Great Britain, including notification of suspected cases, muzzling orders etc. The disease was reintroduced into this country once only since 1917. This was after the armistice in 1918, and was due to a dog or dogs illegally imported by a demobilized soldier, and by others. The consequences were very serious. From 1918 to 1922 there were no less than 325 cases of rabies in animals and there were nearly a thousand suspected cases reported; 358 persons were bitten, 123 of these by dogs known to be rabid, and 144 persons received vaccine treatment.

The conditions which in 1918 facilitated the illegal importation of dogs and other animals have returned in an aggravated form, and it would be rash to assume that the present sequence of 23 years' freedom from rabies (apart from cases in imported dogs in quarantine) will continue unbroken.

It would appear that attention should be drawn on a larger scale to the risks of serious consequences attendant on the criminal evasion of the importation regulations.

In this connexion it is of interest that on the 4th July, 1945, an Order was issued by the Ministry of Agriculture entitled the Importation of Dogs and Cats (Amendment) Order of 1945. This Order allows the importation of dogs under a licence granted by a commissioned officer of His Majesty's Army authorized in that behalf by an assistant Under Secretary of State at the War Office in the case of a dog owned by a member of H.M. Navy, Army or Air Force. Such dogs shall be detained and isolated for a period of six calendar months after landing in Great Britain upon premises which have been approved, for the purpose of such detention and isolation, by or on behalf of the Secretary of State for War and which are under the control of the Royal Army Veterinary Corps.

There will therefore be, in future, two forms of licence under which dogs may be imported into Great Britain, *viz.* :—

(1) That issued by Authorized Army Officers in respect of dogs to which the special scheme applies. These dogs will be detained in the specially provided quarantine kennels.

(2) That issued by the Ministry of Agriculture and Fisheries in respect of any other dogs and cats. These animals will as hitherto be detained in approved quarantine kennels under civilian control.

It will be open to members of the services who do not wish to, or who cannot, take advantage of the special service scheme, to make use of those facilities which are available to members of the general public ; in all such cases the necessary licences must, as hitherto, be obtained from the Ministry of Agriculture.

In a circular letter sent to all local authorities for the purposes of the Diseases of Animals Acts, and to all Chief Constables, the Ministry explains the implications of the Order which has been referred to above, and urges that when particulars of the scheme are published, warnings should be given to members of H.M. Navy, Army and Air Force about the dangers of rabies and of the risks attendant upon the smuggling of dogs or cats into Britain.]

In the *Bulletin*[8] referred to above, information is given on the methods employed in Great Britain for dealing with rabies should cases arise, and the addresses are given of centres from which vaccine for anti-rabies treatment of

human subjects may be procured, and the address to which material collected from suspected cases should be sent for diagnosis. [The reviewer would like to see the more general use of the mouse for more rapid biological diagnostic tests (see this *Bulletin*, 1937, v. 34, 677 ; 1943, v. 40, 652–4) and considers it to be advisable also for vaccines which are intended for anti-rabies treatment to be submitted to potency tests (this *Bulletin*, 1941, v. 38, p. 161). Periodic examination of the characteristics of the fixed strain of virus used for the preparation of the vaccine should also be made. He would also like to suggest the adoption of a better method of sending the material, head and neck or brain and cord, for diagnosis so as to avoid the putrefaction and liquefaction of the nervous tissue to be examined, which so often occurs.]

In the annotation in the *Lancet* referred to above, reference is made to the local treatment of the bites of rabid animals. [It should be pointed out that the sucking of the bite with a view to removing infected saliva as recommended would be a dangerous procedure as it is generally accepted that, on a mucous surface such as the mouth, or where the skin is definitely broken, infection with rabies can occur. There is some evidence also that thorough syringing with a 20 per cent. green soap solution would be as effective as the more drastic method of cauterization (see this *Bulletin*, 1944, v. 41, 173–5, 180 and 912) and with regard to the question of WEBSTER's remarks, on an anti-rabies vaccine treatment referred to in the same annotation, they have been commented on by the reviewer (this *Bulletin*, 1943, v. 40, 269–70 ; 656 ; and 1944, v. 41, 180) with regard to statistical evidence on anti-rabies vaccine treatment in human beings. Webster's scepticism arose from the unsatisfactory results obtained in potency tests on many commercial vaccines in America. He was also justifiably critical of much of the evidence produced in support of the effectiveness of anti-rabies vaccination. Nevertheless what he was striving for was the development of methods of estimating the potency of vaccines and standardization of the biological product. Yet his critical attitude and scepticism would not justify the withholding of vaccine treatment, and indeed he said " persons exposed to rabies should be given treatment with confidence that there is small likelihood of development of the disease." What he implied in his attitude of scepticism was that if anti-rabies treatment was to be applied, the vaccine should be tested in some way for antigenic potency so that the method of treatment should not be condemned because of the use of an inferior product. Webster's attitude is, in the reviewer's opinion, not always correctly interpreted. It would perhaps be opportune to state here that it is felt that it would be extremely useful if there was a centre in Britain for the study of rabies. There are many problems which could be tackled, such as the study of the immunogenic, immunological and other properties of fixed strains of rabies virus, and the methods of estimating the potency of vaccines. Further information is also required on suggested type immunological differences between strains of street rabies virus, and on the nature of the virus and its physico-chemical properties. Such a centre might well work under the aegis of the Medical Research Council and the Agricultural Research Council, and the knowledge which was acquired would be useful also to the Colonial Office and the Ministries of Health and Agriculture. Surely it would be useful also that there should be an instructional centre for medical and veterinary officers proceeding overseas on such an important disease as rabies. It would not be difficult to organize and run such a unit.]

Aujeszky's Disease.

HIRT[11] records that in his experience, swine, inoculated intracerebrally with the virus of Aujeszky's disease contained in a suspension of brain, nearly always

[11] HIRT, G. Infektions und Immunisierungsversuche mit dem Virus des Aujeszkyschen Krankheit. *Arch. wiss. prakt. Tierheilk.* 1942, v. 78, 186–90.

succumbed to the infection ; death ensued in 1 to 2 days after the first symptoms were observed. The incubation period was usually 3 to 4 days, but was occasionally as long as 6 days. There was a sharp but transient rise of temperature 12 to 24 hours before the onset of symptoms. At autopsy gastro-enteritis and oedema of the lungs were sometimes seen, but at other times there were no macroscopic changes. There were some infiltrative lesions in the c.n.s. The virus could be recovered from the blood, spleen and the lung.

Two pigs were inoculated intracerebrally with virus and at the same time they received 50 cc. of an immune serum, one intravenously and the other subcutaneously. The potency of the serum was such that 0·01 cc. neutralized 25 rabbit fatal doses of virus and it was estimated that the 50 cc. dose of serum should have been capable of neutralizing 125,000 rabbit doses of virus. Both pigs died after an incubation period of 6 days, and they died on the seventh and eighth day respectively. Two pigs which had been inoculated many times with virus-infective rabbit brain, and two pigs which had recovered from a spontaneous attack of the disease, were shown to have immune bodies in their sera, and when inoculated intracerebrally with virus all four animals survived.

Hirt,[12] in a second paper, states that 0·1 cc. of a 1 per cent. suspension of virus-infected brain material almost always leads to a fatal inoculation. Eight passages of virus were made intracerebrally in swine and the author records that there was no alteration in the symptoms, the incubation period or duration of the disease. On three occasions during the course of the eight passages, two swine were inoculated, *viz.*, at the fourth, fifth and seventh passages. On two occasions, *viz.*, at the fourth and fifth passages, one pig died and one survived, and the sera of the surviving swine were shown to be capable of neutralizing the virus of Aujeszky's disease. In rabbits, 50 successful passages were made intracerebrally. In another series of passages in rabbits, suspensions of the lumbar cords, inoculated into the thigh muscles, were passaged successfully in series through 40 passages, viz. :—

Virus
↓
Muscle → cord → muscle → cord →
cord → muscle → cord → muscle etc.

1st pass. rabbit	2nd pass. rabbit	3rd passage rabbit

In a third series of passages in rabbits, suspensions of the brains of rabbits, inoculated into the thigh muscles, were passaged in series in the same way, but the rabbits survived after the second or third passages.

In other experiments virus was inoculated into the shoulder muscles of 14 rabbits. All the rabbits developed typical symptoms and died. In all the 14 rabbits, virus in sufficient amount to infect rabbits when inoculated intramuscularly was demonstrable in the cervical cords, but in only six cases in the brain, and in three cases in the lumbar cord. Rabbits were also inoculated intracerebrally with suspensions of the rabbit brains, of which suspensions had failed to infect when inoculated intramuscularly, and negative results were recorded.

[The information contained in the above two papers by Hirt on Aujeszky's disease confirms and extends what is already known about its pathology, to the knowledge of which he has already made valuable contributions—see pages 756, 758 and 759 of a review by Galloway (this *Bulletin*, 1939, v. 36, 195).]

Ian A. Galloway.

[12] Hirt, G. Bei der Aujeszkyschen Krankheit is der Virusgehalt des Zentralnervensystems durch die Infektionsstelle bedingt. *Arch. wiss. prakt. Tierheilk.* 1942, v. 78, 191–4.

MALARIA.

RUSTOMJEE, K. J. **Observations upon the Epidemiology of Malaria in Ceylon.** *Ceylon Sessional Paper XXIV.—1944.* Dec., 32 pp., 5 maps, 8 diagrams & 4 charts. Colombo: Ceylon Govt. Press. [Price 2·50.]

This lengthy report describes the distribution and intensity of malaria in Ceylon and gives a brief account of malaria epidemics in that island with detailed information regarding the incidence of the three species of malaria plasmodia during the epidemics of 1939 and 1943.

Variations in rainfall permit of the division of Ceylon into dry, intermediate and wet zones. The incidence of malaria is high over nearly all the dry zone, except in the hilly areas above 3,000 feet, but epidemics do not occur. Moderate to severe malaria characterizes the intermediate zone. In the wet zone malaria incidence is low but epidemics are liable to occur. Spleen rates were high over the whole island in 1936 as a result of the great epidemic of 1934–35; in the dry zone they remained high, but elsewhere they reached normal levels after one or two years. Similar findings followed the 1939 epidemic. In the absence of epidemics *P. vivax* and *P. falciparum* are about equally prevalent in the wet zone; *P. falciparum* is more prevalent than *P. vivax* in the intermediate zone; in the dry zone *P. malariae* is pre-eminent. Death rates return to normal within two years of a major outbreak, infant mortality rates more quickly still.

Widespread epidemics have occurred at intervals of 4–6 years or slightly longer, and are commonly confined to the wet and intermediate zones. Here the drying up of river beds, consequent upon deficient rainfall, leaving pools favourable to the breeding of *A. culicifacies*, favours epidemic prevalence. Excessive rainfall and floods may cause increased malaria incidence in the malarious dry zone but not elsewhere. The months of April to June, and October to December, are the seasons of most frequent epidemic manifestations in the wet and intermediate zones. The season of maximum malaria prevalence in the dry zone is October to February. No precise measurements of any of the numerous factors involved in the causation of epidemics have as yet furnished reliable data for forecasting such epidemics with any degree of reliability.

During the spring epidemics of 1939 and 1943 *P. vivax* was more prevalent than *P. falciparum* in the wet zone, while the reverse was the case in the intermediate zone. *P. malariae* played no part in the epidemic manifestations in either zone.

A complete summary of the large amount of information contained in this report is not possible. *Norman White.*

GEIGY, R. Malaria in der Schweiz. [**Malaria in Switzerland.**] *Acta Tropica.* Basle. 1945, v. 2, No. 1, 1–16, 11 figs. [17 refs.]

According to GALLI-VALERIO there were many foci of malaria in Switzerland in the first half of the 19th century, and it is remarkable that, as in Sweden and Finland, some time between 1870 and 1890, one focus after another died out although the anopheline mosquitoes remained unchanged in numbers and distribution. This was not due to greater severity of climate during that period, but many sanitary works were carried out and more medical treatment was given. Other possible influences were the increase of cattle (resulting in the attraction of the mosquitoes away from man and tending to increase zoophily), and, as GALLI-VALERIO suggested in 1901, the development of immunity on the part of the mosquitoes against *Plasmodium vivax*. The last question has

been investigated by the author at Basle, where a group of interned persons suffering from benign tertian malaria, acquired mostly in Sardinia, were under medical care.

The chief anophelines to be considered were *A. maculipennis* var. *typicus* and *A. bifurcatus*. A small station was established in Basle University in July 1944, and adult mosquitoes from several of the old malaria foci were obtained; very little breeding out from eggs and larvae was done. Although the mosquitoes were kept in warm surroundings, the hibernating state was evident by the end of October. All male and many female *A. maculipennis* die, a few fertilized females with immature ovaries survive, and no larvae can be found; all adult *A. bifurcatus* disappear, but larvae from the latest deposited eggs reach stage 3 or 4 and survive the winter, being found in frozen ponds and slowly flowing streams.

According to Sautet [*Ann. de Parasitol*, 1933, v. 11, 161] the stage 4 larva of *A. bifurcatus* can be stimulated to develop into the imago by means of potassium permanganate or chlorinated water, but experiments by the present author, with this aim, were completely unsuccessful, all the larvae dying. When the larvae are simply kept at room temperature, an occasional imago emerges but they are too few for practical use.

Mosquitoes, caught chiefly in cattle houses, fed at once on man, showing no sign of possessing any firm zoophily. After feeding they were kept at 24°C. The results are shown in the following table:—

Sporogony researches (3rd August to 8th December, 1944)

	A. maculipennis	*A. bifurcatus*	Total
1. Mosquitoes used	69	113	182
2. Placed once on a gametocyte carrier (no infection)	27	15	42
3. Placed many times on a gametocyte carrier	42	98	140
4. Infected (8·6 per cent.)	6	6	12
5. Oöcysts in stomach only	1	5	6
6. Infection of salivary glands only ...	2	—	2
7. Both stomach and glands	3	1	4

Ciuca *et al.* (*Acad. Roumaine Bull. Sect. Sci.*, 1942, v. 25, 96) had previously found with *P. falciparum* and *A. maculipennis* var. *atroparvus*, that repeated feeds produced a higher rate of infection than single feeds. In the present experiment, the shortest time between feeding and finding cysts in the stomach wall was 10 days; it was often 20 or more days before the salivary glands became infected. In three cases the different ages of the cysts showed that superinfection had occurred. The infected mosquitoes were not used to reinfect man but the sporozoites were active and probably infective. One of the most heavily infected stomachs showed 400 cysts.

The stomachs and glands were examined in Ringer's solution and were fixed in Duboscq fluid, Carnoy fluid, or sublimate-alcohol-acetic acid mixture; sections were stained with Heidenhain's haematoxylin.

The material was insufficient for a close cytological study. No difference was observed in the evolution of the cyst in the two species of mosquito. Mitosis

was not seen in the development from a uninuclear to a quadrinuclear cyst ; further development agreed with textbook descriptions.

The infection of the glands varies ; all three lobes may be swollen, or the diverticula may be very slightly expanded and difficult to distinguish from a normal gland.

The author discusses the epidemiology of malaria in Switzerland and gives various reasons for concluding that there is little chance of its again becoming prevalent.

The paper is illustrated by excellent photographs. *J. F. Corson.*

YOUNG, M. D. **Studies on the Periodicity of Induced** *Plasmodium vivax*. *J. National Malaria Soc.* Tallahassee, Fla. 1944, Dec., v. 3, No. 4, 237–40.

The assumption that paroxysms of *P. vivax* malaria have a periodicity of exactly 48 hours is not true for some strains of that parasite. The majority of the observations recorded in this paper were carried out on the St. Elizabeth strain of *P. vivax* which is used in the South Carolina State Hospital for the treatment of neurosyphilis. Patients exhibiting a tertian type of fever, indicative of a single brood of parasites, were selected. Measurements were made of the intervals between one fever peak and the next. The patients' temperatures were taken four-hourly ; hourly when over 100°F. The peak of the segmentation of the parasites precedes the peak of fever by several hours, the peak of fever coinciding closely with the peak of young ring forms. Of such observations 307 were made in patients who had been infected by injection of infected blood, and 94 in patients who had been infected by mosquito bite. There was no significant difference between the paroxysmal intervals in these two groups of patients. The average interval was 43·42 hours.

Twenty-five similar observations were made on two patients infected with a strain of *P. vivax* contracted in the New Hebrides. The average paroxysmal interval was 45·76 hours.

Sixty-four paroxysmal intervals in patients infected with a strain of *P. vivax* used for malaria therapy in Baltimore averaged 41·52 hours.

The results indicate that different strains may each have a characteristic periodicity which would be of value in distinguishing such strains.

Norman White.

BIRD, J. **Malaria Eradication by breaking the Sporogonic Cycle of the Plasmodium. Preliminary Note.** *Bol. Asoc. Med. de Puerto Rico.* 1945, Feb., v. 37, No. 2, 56–7.

As the tissues of anopheline mosquitoes are the natural medium in which the sexual cycle of development of malarial parasites takes place, it occurred to the author that the injection into man of an antigen prepared from the mosquitoes might stimulate the formation of antibodies having the power of preventing the development of gametocytes. He ground up 1 gm. of anopheline mosquitoes in 100 cc. of distilled water, and filtered through filter paper and then through a Berkefeld filter. A dose of 2–4 cc. of this filtrate, repeated 2–3 times at 8-day intervals, was injected intramuscularly into volunteers and patients with syphilis of the nervous system. They were afterwards infected with malaria by inoculation of blood containing schizonts ; in some cases no gametocytes were found and in others only male gametocytes. The author therefore concluded that the sporogonic cycle had been broken by this means. [No details of the experiments are given in this preliminary note.]

J. F. Corson.

Russell, P. F., Knipe, F. W., Ramachandra Rao, T. & Patnam, P. **Some Experiments on Flight Range of** *Anopheles culicifacies*. *J. Exper. Zool.* Philadelphia, Pa. 1944, v. 97, No. 2, 135–63, 13 figs. [15 refs.] [Summary taken from *Rev. Applied Entom.* Ser. B. 1945, May, v. 33, Pt. 5, 71.]

The following is based on the authors' summary and conclusions. Nine experiments on the flight-range of *Anopheles culicifacies*, Giles, were carried out in Madras between 22nd July and 28th October 1941. Mosquitos marked with coloured dust were released at a point around which 80 calf-baited traps were arranged in concentric circles with radii of $\frac{1}{4}$, $\frac{1}{2}$, $\frac{3}{4}$ and 1 mile. The larger circles had, respectively, two, three and four times as many traps as the smallest so that the traps were the same distance apart on each circle. Some 207,800 mosquitos were collected in the traps and in villages just beyond them and examined for evidence of coloured dust. The greatest observed flight-range was between 1·5 and 1·75 miles. Nine mosquitos flew this distance in a night and seven others in two nights. Three of the flights were against the wind.

The object of the study was to find a basis on which to fix the limits of the zone in which anti-mosquito measures are necessary for malaria control. The data obtained were analysed statistically. If the flight-ranges of the mosquitos released had been random, a similar proportion should have been taken on the periphery of each of the four zones of the experimental field. The observed dispersion never achieved this, and it must be concluded that inhibiting factors prevented a random distribution of flight-ranges. The relationship between mosquito captures (y) and distance proved to be hyperbolic with an equation of the form $y=a \div x^b$, where x is the distance in miles from the point of release, a is the number of mosquitos expected on the circle with radius of 1 mile and b is the measure of flight-inhibiting factors. The value of a is determined primarily by the number of mosquitos released. The value of b is a measure of the extent to which the flight ranges of a specific group have been inhibited. Thus the b value for males of *A. culicifacies* (1·602) was greater than that for females (0·681). Mosquitos flying with the wind were less widely dispersed than those flying across or against the wind. Mosquitos taken in nature flew greater distances than those bred in the laboratory, although the difference between the b values for the two groups was not significant.

It is pointed out that although the effect of flight-inhibiting factors has been defined for the various groups of Anophelines recaptured, it may not be maintained very far beyond the 1-mile limit; that, owing to the wide fluctuations of the observed captures, estimates based on the equations for distances within the 1-mile zone are subject to a considerable standard error; and that effective female flight-range leading to malaria transmission is dependent on the number of females coming to rest in human habitations. Adjustments must be made of density estimates based on animal-trap catches before such a figure can be obtained.

Huffaker, C. B. & Back, R. C. **A Study of the Effective Flight Range, Density, and Seasonal Fluctuations in the Abundance of** *Anopheles quadrimaculatus* **Say in Delaware.** *Amer. J. Trop. Med.* 1945, Mar., v. 25, No. 2, 155–61, 5 figs. [14 refs.]

A. quadrimaculatus is very abundant at Fort duPont, Delaware, but its breeding places are almost exclusively confined to two large freshwater marshes. Four cattle barns were selected at each of six distances from the nearest point of major breeding, each distance was therefore replicated four times. On an average, 17 inspections were made of each barn during the summer, with the following results:—At 0·1 miles from the breeding centre an average of 4,963

anophelines were captured per inspection; at 0·5 miles, 2,506; at 1·0 miles, 250; at 1·5 miles, 10; at 2·0 miles, 4; and at 3·0 miles 3. The following is quoted from the author's summary.

"*A. quadrimaculatus* does not move in significant numbers more than 1 mile from its breeding sources. However, an unusual condition is described where this species was observed to move 1 mile from its breeding areas in sufficient numbers to create a dangerous density—250 females per barn or shed per inspection. Near the sources of production, densities as high as 15,000 to 25,000 females per station per inspection are noted as very common, and one such record of 40,000 is included. In the study-locality (Fort duPont, Delaware) broods of this species are indicated at about monthly intervals during the summer season." *R. M. Gordon.*

KNIGHT, K. L. & FARNER, D. S. **A Correction in Anopheline Nomenclature (Diptera : Culicidae).** *Proc. Ent. Soc. Wash.* Washington, D.C., 1944, v. 46, No. 5, 132–3. [Summary taken from *Rev. Applied Entom.* Ser. B. 1945, May, v. 33, Pt. 5, 79.]

The authors conclude from a study of the literature and of material collected over a period of more than a year in the coastal areas of the Islands of Efate and Espiritu Santo and on one occasion on Mallicolo Island that the subspecies or variety of *Anopheles punctulatus*, Dön., known as *moluccensis*, Sw. & Sw., in the New Hebrides, and in which the proboscis, excluding the labella, is entirely dark, should be designated *A. punctulatus farauti*, Lav. It was the only form seen there. It is not possible to say whether *A. p. moluccensis* is a synonym of *farauti*, but it is anticipated that this will prove to be the case. Examination of several hundred specimens from the Solomon Islands and eastern New Guinea supports the theory, but de Rook indicates that a considerable variation in the colour of the proboscis exists in western New Guinea, where most of the females determined by him as *moluccensis* have a ventral pale area on the apical quarter of the proboscis.

PARENT, M. & DUMOULIN, M. L. La faune anophélienne à Yangambi (Inéac). Biologie *A. moucheti* Evans spécialement. Applications statistiques. [**The Anophelines of Yangambi : Biology of** *A. moucheti*.] *Rec. Travaux. Sci. Méd. Congo Belge.* 1945, Jan., No. 3, 159–73, 2 figs.

PERYASSÚ, A. Os *Kerteszias* na epidemiologia da malaria. [**Anophelines of the Sub-Genus** *Kerteszia* **in the Epidemiology of Malaria.**] *Folha Méd.* 1943, Dec. 5, v. 24, No. 23, 213–15.

Two species of the sub-genus *Kerteszia* are found in the mountains and coastal areas of Brazil, *A.* (*K.*) *cruzi* and *A.* (*K.*) *bellator*. Both are of importance in the epidemiology of malaria. The author describes the distinguishing morphological features of these two species and of *A.* (*K.*) *boliviensis*, and summarizes the considerable literature concerning their habits and the rôle they play in the transmission of malaria. *A.* (*Kerteszia*) *cruzi* Dyar and Knab 1908, is synonymous with *Anopheles lutzii* Theo. (1901) and with *Myzomyia lutzii* Peryassú 1908. *Norman White.*

OFFICER, R. **Experimental Transfusion with Malaria Infected Blood.** *Med. J. Australia.* 1945, Mar. 17, v. 1, No. 11, 271–4, 1 fig.

It has long been known that malaria produced by the injection of infected blood is readily controlled by quinine, but warnings have frequently been published against the use of potentially malaria infected individuals as donors

for blood transfusion. The experiments described were carried out to determine whether the malaria acquired by blood transfusion can be readily controlled, and whether the immediate harmful effects are such as to nullify the benefit of transfusion.

Five healthy volunteers who had never lived in malarious areas were the subject of experiment. Blood sufficient in amount to contain 300,000,000 parasites was drawn from a malaria patient and mixed with 560 cc. of citrated blood from a compatible non-malarial donor. The subject of experiment was then bled to an amount of 750 cc., or until signs of collapse were noted. The malaria-infected blood was then given by the drip method. All volunteers were given antimalarial treatment immediately after the transfusion, the routine course of malaria therapy being used in most cases. None of the volunteers developed malaria and no immediate effects were noted. Remote effects, slight to moderate pyrexia lasting one to three days—rarely began before 24 hours had elapsed, and were never serious enough to cause alarm. It is concluded that in a case of emergency a potentially malarial donor can be used for transfusion with the knowledge that the benefit from transfusion would far outweigh possible ill effects. Such blood would contain less numerous parasites than did the blood used in these experiments. *Norman White.*

RIGDON, R. H. **A Consideration of the Mechanism of Splenic Infarcts in Malaria.** *Amer. J. Trop. Med.* 1944, Nov., v. 24, No. 6, 349–54, 7 figs. [14 refs.]

A study of the spleens of man infected with *P. falciparum*, of monkeys infected with *P. knowlesi*, of canaries infected with *P. cathemerium*, and of ducks infected with *P. lophurae*, has led to the conclusion that the infarcts occurring in the spleen in malaria may result from an obstruction produced by hyperplasia of the reticular-like cells in the walls of the venous sinuses. Leucocytes and red blood cells may adhere to the surface of these masses of reticular-like cells. This process is facilitated by the slowing of the blood current resulting from anaemia and anoxia of the cardiac muscle. Associated with anoxia there may be also an increase in capillary permeability. The hyperplasia of the cells in the wall of the veins is a part of the general process of hyperplasia of the splenic pulp.

[Observations on the adhesion of red cells to each other and on the adhesion of leucocytes to capillary endothelial cells were reported by KNISELY, *et al.*, this *Bulletin*, 1943, v. 40, 584, and may have a bearing on the subject.]

Norman White.

HEIDELBERGER, M. & MAYER, M. M. **Normal Human Stromata as Antigens for Complement Fixation in the Sera of Patients with Relapsing Vivax Malaria.** *Science.* 1944, Oct. 20, 359–60.

It was noted by KLIGLER and YOELI [this *Bulletin*, 1942, v. 39, 255] that the sera of certain malarial patients fixed complement with antigens prepared from normal chicken erythrocytes. The authors of the present note find that these sera fix complement even more readily when an antigen prepared from normal human erythrocytes is employed. Furthermore, many sera from malarial patients which fail to react either with *Plasmodium knowlesi* or *P. gallinaceum* antigens or with normal chicken erythrocyte antigen fix complement strongly with the human erythrocyte antigen. On the whole it may be stated that the readily available normal human stromata are about as sensitive as the *P. gallinaceum* antigen, which is expensive and not easily accessible. Thus, of 167 sera from malarial patients, 22 per cent. were positive with the latter antigen and 28 per cent. with the former. Of 32 normal sera and 81 pathological

sera tested as controls with the human erythrocyte antigen, only four probable false positives were found, in all of which a malarial factor was unlikely to have been the cause. A fuller account of the observations is promised.

C. M. Wenyon.

POTTER, H. W., BRONSTEIN, L. H. & GRUBER, C. M. **Blood and Spinal Fluid Tests for Syphilis in Malarial Patients.** *J. Amer. Med. Ass.* 1945, Mar. 24, v. 127, No. 12, 699–701.

In view of the known fact that false positive serum tests for syphilis are not uncommon in malarial patients, the authors tested the blood and c.s.f. of 100 consecutive "malaria admissions" within 48 hours of entrance to hospital. [It is not stated how many of these patients were pyrexial at the time.] All were without history of syphilis, and had had at least one negative serum test for syphilis (and often several) and had passed at least 24 physical examinations; it can be assumed, therefore, that they were all non-syphilitic. Of the 100 sera 12 gave a positive reaction to the Wassermann and/or Kahn test and 10 a doubtful reaction to one or both tests, as shown in the following table :—

	Positive Tests		
Kahn positive	... Wassermann positive	...	3
Kahn positive	... Wassermann doubtful	...	2
Kahn positive	... Wassermann negative	...	2
Kahn negative	... Wassermann positive	...	5
	Total	...	12
	Doubtful Tests		
Kahn doubtful	... Wassermann doubtful	...	4
Kahn doubtful	... Wassermann negative	...	1
Kahn negative	... Wassermann doubtful	...	5
	Total	...	10

The spinal fluid W.R. was negative in all cases; in one fluid there were 17 cells—6 polymorphonuclears and 11 lymphocytes per cmm.; in 3 cases the total protein was 75 mgm. per 100 cc. All other tests, including the Lange, were within the bounds of normality.

All serum reactions returned to negative within 30 days, with an average of about 12 days; many did so in seven days or less. All the patients had *Plasmodium vivax* infections, except one in whom the infection was with *Plasmodium falciparum*. Another table, as follows, shows the correlation of the duration of infection and area of origin with the serological test :—

Result of Test in Relation to Origin of Infection

Area	Cases	Positive	Doubtful	Average duration of infection: months
Solomon Islands	49	3	5	17
Mediterranean ...	32	5	3	9
New Guinea ...	13	3	2	9
Panama ...	4	0	0	
West Africa ...	1	0	0	
Central Africa ...	1	1	0	
Total ...	100	12	10	

The conclusion to be drawn is that the physician should be wary of diagnosing syphilis on the result of one test, and if the patient has had malaria, particularly so ; a repeat test should be done after a month. [Most people consider that tests, if positive, should be carried out over even longer periods.]

T. E. Osmond.

MERRILL, B. R. **Psychogenic "Malaria."** *U.S. Nav. Med. Bull.* 1945, Jan., v. 44, No. 1, 69–72.

The author has observed several patients in whom what appeared to be malarial chills proved to be anxiety attacks. In each instance *P. vivax* malaria had been contracted in the South Pacific and in each case the malaria had run a refractory course with numerous recurrences. The patients were psychologically attuned to frequent true malarial chills. Such a patient enters hospital stating that he has had a malaria chill. Shortly after admission he has another "chill" which resembles a malarial attack, but there is no elevation of temperature. No plasmodia can be found. The patient resents the information that he is not suffering from malaria. The psychological history in these cases is one of psychopathic behaviour from early youth. The patient's outstanding conflict in life has been his inability to control his aggressive tendencies even before the intense accentuation of this conflict brought about by fighting and military discipline. With a sufficiently slow and tactful approach these patients may be made to accept the psychogenic nature of their symptoms ; the "chills" then disappear. There remains, however, a personality that has difficulty in adjusting itself to the social restraints of civilian life. The ultimate prognosis depends more on the severity of the personality defect prior to the exposure to battle than on the severity of combat experience. Psychotherapeutics of these cases are difficult largely because the psychogenic factors were so effectively concealed behind the diagnosis of malaria at the time when psychotherapy would have been most effective.

Norman White.

VISWANATHAN, R. **Cerebral Malaria : Pathogenesis, Symptoms and Treatment.** *Indian Med. Gaz.* 1944, Oct., v. 79, No. 10, 455–8, 5 figs. on pl. 21.

During a period of 4 months 2,256 cases of malaria were treated, of which 996 were *P. falciparum* infections. Of the latter 44 patients developed cerebral symptoms ; eight of them died in spite of energetic anti-malaria therapy. The symptomatology of the cerebral cases is described and case reports are given of the eight fatal cases, together with macroscopic and histological post-mortem findings. All this is preceded by a discussion of the pathogenesis of cerebral malaria. The author's observations lead to the conclusion that primary damage to capillary endothelium is caused by malarial toxin and that this leads to clumping of cells and pigment ; the presence of parasites in the cells is immaterial. The slowing of circulation due to the fall of blood pressure in the later stages of cerebral attacks facilitates the process of thrombosis, and irreparable and irreversible damage is done to the brain tissue. In five of the fatal cases a well-formed ante-mortem clot was found in the sagittal sinus. The author believes that sinus thrombosis in cerebral malaria has not hitherto been reported.

All the non-fatal cases of cerebral malaria ended in complete recovery.

[For a description of the pathological findings in cerebral malaria, and a discussion of the processes involved, see DHAYAGUDE and PURANDARE, this *Bulletin*, 1944, v. 41, 533.]

Norman White.

Gordon, H. H., Lippincott, S. W., Marble, A., Ball, A. L., Ellerbrook, L. D. & Glass, W. W., Jr. **Clinical Features of Relapsing *Plasmodium vivax* Malaria in Soldiers Evacuated from the South Pacific Area.** *Arch. Intern. Med.* 1945, Mar., v. 75, No. 3, 159–67, 5 figs.

The observations concern 435 soldiers evacuated to the United States from islands in the South Pacific mostly on account of frequent relapses from malaria. All but seven were white ; all were young adults ; with the exception of 20 none had suffered from malaria prior to exposure to infection in the South Pacific ; all had had suppressive treatment in the Pacific, mostly with quinacrine hydrochloride [mepacrine], 0·4 or 0·6 gm. weekly ; all had had prompt treatment of acute attacks ; all but four had had acute attacks prior to admission to the Harmon General Hospital where these observations were made (and where the incidence of indigenous malaria is extremely low) ; all were observed from one to seven months ; *P. vivax* alone was found in all but one patient, in whom *P. falciparum* was also identified.

The strain or strains of *P. vivax* were characterized by a very pronounced tendency to relapse, and to the relative mildness of the acute attacks they caused. Of 49 men the duration of whose infection was from 13 to 16 months, 37 per cent. had had from 10 to 12 attacks, 12 per cent. had had from 13 to 16 attacks and two men had had more than 16 attacks.

The symptoms displayed by these patients are analysed in some detail. Chill was experienced in 80 per cent. ; headache, weakness and malaria in 96 per cent. ; abdominal pain in 47 per cent. ; nausea in 59 per cent. ; vomiting in 36 per cent. ; herpes labialis in 27 per cent. Cerebral symptoms were conspicuously infrequent, and when they did occur were probably conditioned as much by the previous personality of the patient as by the effects of the malaria attack. Splenomegaly was not marked ; the spleen was felt in 23 per cent. of acute attacks but then only transiently.

Most of the clinical attacks were treated with quinacrine hydrochloride, 0·2 gm. every six hours for five doses then 0·1 gm. thrice daily for six days. In only one patient was the response to quinacrine given by mouth unsatisfactory.

A programme of rehabilitation was instituted, with great benefit to the development of physical stamina and the restoration of self-confidence.

Norman White.

War Office. Army Med. Dept. Bull. No. 48. 1945, June, 6–7. **Drugs for Relapsing Vivax Malaria.**

" Radical cure of malaria is the permanent elimination of infection and the criterion for its attainment is freedom from relapses.[1] Anti-malarial drugs vary in their ability to produce a radical cure and their effectiveness in this respect can be tested by comparing relapse rates after different forms of treatment. Reinfection will obscure the anti-relapse properties of the best drug ; therefore trials were carried out in the United Kingdom on men returned from the Central Mediterranean Force who developed relapses of malaria. Practically all relapses were due to *vivax* (B.T.) malaria since continued use of mepacrine for 3–4 weeks after leaving the malarious area had eliminated *falciparum* (M.T.) malaria ; only proved cases of relapsing B.T. malaria are considered here. During May and June, 1944, 1,410 such cases were treated with one or other of the two courses below :—

" (1) *Mepacrine* (*M*) *course.*—0·2 gram of mepacrine was given every six hours for 48 hours—then 0·1 g. three times a day for 10 days. The course lasted 12 days and the total amount of mepacrine was 4·6 g.

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[1] This *Bulletin*, 1945, April, Supplement No. 21.

" (2) *Quinine pamaquin (QP) course.*—Quinine, grains 10 and pamaquin, 0·01 gram were given three times a day for ten days.

" Records were examined after a follow-up five months later.[2] In 176 of the patients the first attack of malaria developed after their return to this country. Of these, 100 were treated with course M and 29 subsequently relapsed; 76 were treated with the QP course and only 14 relapsed within the period of observation.

" The difference between these relapse rates is statistically significant; this means that the odds are heavily against such a result having happened by chance alone and, other things being equal, strongly suggests that the QP course of treatment was the more effective in preventing relapses.

TABLE.—*Relapses of vivax (B.T.) malaria after treatment with mepacrine or quinine-pamaquin courses.*

Relapses after treatment	Course M		Course QP	
	No. of cases	Percentage of all cases	No. of cases	Percentage of all cases
None	429	66·0	524	89·7
1	184	28·3	56	9·6
2	33	5·1	4	0·7
3	4	0·6	0	—
Total relapsed cases ...	221	34·0	60	10·3

" Men whose first attack had developed abroad formed a much larger group (1,234 cases). They also were treated with course M (650 cases), or course QP (584 cases) and again the follow-up showed fewer relapses after QP treatment; the findings are given in the table.

" Further analysis revealed an unexpected event—namely, that relapse after the QP course, when it did occur, was earlier than after course M; the explanation of this difference is not known although, in part at least, it may be due to the slower excretion of mepacrine.

" This follow-up was carried out five months after the patients had been treated; so far, the QP course appears to have been more successful than course M, but it is too early to say that radical cures have been obtained since BT relapses may occur up to two years after the last infection.

" Two points of importance must be borne in mind in treating patients with the QP course. The first is that the patient must be kept under strict medical supervision throughout treatment and if cyanosis or abdominal colic appears, pamaquin should be discontinued and the course completed with quinine only; only some 2–4 per cent. had to have treatment interrupted in this way. The second is that Indian troops do not tolerate pamaquin as well as British; for this reason, Indians should receive only 0·02 g. instead of 0·03 g. of pamaquin daily. Pamaquin haemoglobinuria has been described in Indians; it appears usually on the 4th or 5th day after pamaquin has been started. It should be treated like blackwater fever."

[2]War Office. 1945, *D.B.R. Interim Report on Malaria Relapses after Treatment with Quinine and Synthetic Quinine Substitutes.*

SINTON, J. A. **The Principles governing the Curative and the Suppressive Treatments of Human Malaria, with special reference to Military Conditions.** *J. Roy. Army Med. Corps.* 1945, Apr., v. 84, No. 4, 147–58. [16 refs.]

A successful chemotherapeutic attack upon the gametocytes or sporozoites of malaria in man would be prophylactic, preventing the transmission of infection either to the mosquito or man. A similar attack upon any stage of the asexual cycle of the parasite would be a curative action. In discussing malaria therapy exact definitions should be given of the terms used.

Direct gametocyte prophylaxis is the prevention of the development of infection in the insect vector by the direct destruction, sterilization or devitalization of the gametocytes before they leave the human host.

Indirect gametocyte prophylaxis refers to the temporary reduction in the number of gametocytes or the temporary elimination of these forms in the peripheral blood, by the destruction of the asexual parasites from which they derive.

Eventual gametocyte prophylaxis is the permanent elimination of gametocytes by the complete eradication of the schizogonic forms from which they derive.

True causal prophylaxis entails the radical destruction of all introduced sporozoites, or the hypothetical cryptozoites.

Suppressive treatment is designed to prevent the development of clinical malaria by means of continued drug treatment.

Clinical cure is the cure of clinical manifestations of malaria.

Radical cure is the permanent elimination of infection.

In the light of these definitions the action of the commonly used anti-malarial drugs—quinine, mepacrine, and pamaquin is described. Reference is made to experience in highly malarious areas in New Guinea where it has been shown that the administration of 0·1 gm. of mepacrine every day without fail to all personnel enables a military force to maintain itself in the field with a very low malarial attack incidence.

The applications of the principles of malaria therapy under different conditions of military service are thus summarized :

For non-infected individuals coming to reside in an area where the chances of acquiring malaria infection are slight, no suppressive treatment is necessary ; primary acute attacks should be submitted to radical treatment of short duration, with occasional gametocyte therapy for *falciparum* infections ; relapsing infections necessitate a repetition of the standard course, special treatment being required for chronic *vivax* infections.

For individuals coming to reside in a non-malarious or slightly malarious region from a highly malarious one, and if the period of absence from risk of heavy infection is likely to be prolonged, suppressive treatment may be stopped after four weeks. Primary acute attacks and relapsing infections should, however, be treated as in the previous category. If the period of absence from the risk of heavy infection is likely to be short, suppressive treatment should be continued without cessation.

For individuals exposed to constant and frequent infections, reinfections and superinfections, the treatment should vary in accordance with their state of immunity to malaria. If much malaria sickness occur in an immune or salted population, suppressive treatment with mepacrine in moderate doses should be given ; this can often be discontinued after a few months. Attacks of fever should be so treated as to secure a rapid clinical, but not radical, cure. Gametocyte therapy, or light suppressive treatment is sometimes indicated to protect adjacent non-immune troops. For non-immune or partly immune troops in such conditions, continuous suppressive treatment in full doses should be given,

even if there be a break in the malaria transmission season ; attacks should be treated with a short intensive course. *Norman White.*

MEASHAM, J. E., YOELI, M. & FINNEGAN, J. D. **An Inquiry into the Prophylactic, Suppressive and Curative Properties of Mepacrine (Atebrin).** *J. Roy. Army Med. Corps.* 1945, Apr., v. 84, No. 4, 188–91.

Seventeen patients in a mental hospital in Lebanon were the subjects of the inquiry. Eight received a three weeks course of suppressive mepacrine, 0·4 gm. twice weekly. At the end of this period they were infected with Palestinian or Syrian strains of *P. vivax* by mosquito bites, *A. sacharovi* and *A. superpictus*, and by subsequent subcutaneous injection of the remaining sporozoites obtained by dissection in saline. The patients continued the suppressive treatment for another month during which a second dose of sporozoites was administered to each.

A second group of eight patients, similarly infected, only started their suppressive treatment on the day of their experimental infection.

The remaining patient was a control ; he received one injection of sporozoites but no suppressive treatment.

Five patients of the first group and three of the second group developed clinical malaria, all but one after the cessation of the suppressive treatment.

The field observations reported concern a battalion of Indian infantry in a highly malarious frontier zone where anti-larval measures were not possible. Another battalion stationed in the same area in the previous year in exactly similar conditions had received no suppressive treatment : it suffered severely from malaria, 130 cases of malaria being reported in a single week of July. The battalion under observation was on carefully controlled suppressive mepacrine treatment ; only two cases of malaria occurred. On withdrawal to a healthy camp half the strength ceased taking mepacrine immediately ; the other half continued taking it for a further month. Malaria cases in the former group equalled 17 per cent. of strength ; there was no case among the men who continued the suppressive treatment for a month after removal from the malarious area. [It is not stated if *P. falciparum* infections were common in this area, or if the malaria which occurred after the cessation of mepacrine suppression was due entirely to *P. vivax*.]

The following conclusions are reached :—Mepacrine is not a true prophylactic but it is a useful suppressant. If continued for a sufficient period mepacrine cures infections at a subclinical level. *Norman White.*

THOMPSON, J. H. **Large Initial Doses of Atebrine in the Treatment of Benign Tertian Malaria.** *J. Trop. Med. & Hyg.* 1944, Dec.–Jan. 1945, 3 pp.

This is an account of the treatment of a hundred American soldiers who had contracted malaria in the Mediterranean area and who developed clinically active *P. vivax* malaria after their transfer to a non-malarious temperate clime. All but four gave histories of having suffered from malaria during the previous summer, but their transfer was not made on health grounds. It was not possible to distinguish relapses from latent infections. In the 100 cases the histories revealed an average of 2·4 relapses since the first attack six to nine months previously, the number of relapses varying up to twelve.

Seventy-eight patients received unusually large doses of atabrine [mepacrine] an initial dose of 0·6 gm. followed by 0·2 gm. after each meal for six doses, and then 0·1 gm. thrice daily for seven days. The remaining 22 patients received 0·2 gm. every four hours for five doses and then 0·1 gm. thrice daily for five days.

Atabrine was always given after meals, and if the initial dose had to be given before meal time it was preceded by a pint of chocolate milk, fruit juice or egg nog.

During a two-month period eight patients relapsed; of these only three, 4 per cent., had received the large initial dose of atabrine.

There were no toxic manifestations in any case sufficiently severe as to necessitate stopping the medication; 15 per cent. had mild abdominal cramp after the initial large dose; 6 per cent. had mild diarrhoea easily controlled by paregoric. No patient had mental symptoms.

The eight patients who relapsed were given an initial dose of 1 gm. of atabrine, followed by 0·2 gm. every four hours for six doses and then 0·1 gm. thrice daily for a week. About 6 hours after the 1 gm. dose the patients had severe chills. Before that, marked disintegration of the parasites was observed; clumping of pigment in the plasmodia was observed as early as 45 minutes after the taking of the large dose. Four of the patients had nausea, one had marked diarrhoea and one had mental symptoms with high fever, both transitory. This large 1·0 gm. initial dose should be reserved for selected cases. The optimum time to give a large initial dose is 24 hours after a chill when the patient is having tertian fever. *Norman White.*

SMITH, G. C. & PASSALACQUA, L. A. **Treatment of Acute Malaria with Heavy Doses of Atabrine,** *Bol. Asoc. Med. de Puerto Rico.* 1944, Sept., v. 36, No. 9, 390–97. [14 refs.]

The authors report favourably on the treatment of 10 cases of acute malaria with large doses of atabrine [mepacrine]. During the first 24 hours of treatment the patients received 1·2 gm. of the drug, four doses each of 0·3 gm. During the following four days another 1·2 gm. are given, the total amount given in the five day treatment being 2·4 gm. With this treatment half of the patients with *P. vivax* infections had only one day of fever. The results compared favourably with those obtained by quinine treatment, 10 grains thrice daily for five days and then once daily for five days. Eighty-nine per cent. of the mepacrine patients with *P. vivax* infection had neither fever nor symptoms of malaria after the first forty-eight hours. Mepacrine was never given on an empty stomach; tea or fruit juice with much sugar was given before the drug was administered. *P. falciparum* infections did not respond to mepacrine as rapidly as did *P. vivax.* *Norman White.*

See also p. 753, MARRIOTT, **Medical Problems of South-East Asia Command.**

KAY, C. F. **Failure of Mapharsen as an Adjuvant to Atabrine in the Treatment of Relapsing Tertian Malaria.** *J. Amer. Med. Ass.* 1945, Apr. 14, v. 127, No. 15, 984, 1 chart.

In the Far East 176 patients suffered from relapsing *P. vivax* malaria during a period in which the incidence of fresh infections was insignificant, January to March inclusive. Of these, 109 were treated with atabrine [mepacrine], 0·2 gm. every six hours for five doses, then 0·1 gm. thrice daily for six days. A further relapse occurred in 74·3 per cent. of these patients during the 65- to 140-day period of observation.

In addition to this mepacrine treatment 67 patients were given three intravenous injections of mapharsen, 0·04, 0·06 and 0·06 gm., on the third, fifth and eighth days of mepacrine treatment; 71·6 per cent. of these patients relapsed again. Very early further relapses were slightly more frequent in the group treated by mepacrine alone.

It is concluded that mapharsen given in the above dosage is of no value as an adjuvant to mepacrine in the treatment of relapsing *P. vivax* malaria.

Norman White.

Dao, L. Luis. Resultados clinicos obtenidos con el Mafarside en el tratamiento del paludismo. [**Clinical Results obtained with Mapharside in the Treatment of Malaria.**] *Rev. Policlinica Caracas.* 1944, Sept.–Oct., v. 13, No. 78, 339–49, 2 figs. English summary.

The author reports favourably on the value of mapharside as an antimalarial drug. Sixteen patients with acute malaria, 15 *P. vivax* and one *P. falciparum* infection, were treated. Each patient received three intravenous injections, the adult doses being 0·04 gm. for the first injection and 0·06 gm. for the other two. The interval between the first and the second injection was four days, and between the second and third five days. The results were favourable in all the *P. vivax* infections ; in 13 cases the fever ceased after the first injection. Only three of the patients suffered from a relapse during a two-month period of observation after the end of treatment. The patient with the *P. falciparum* infection developed serious symptoms and received quinine therapy.

Twelve patients with relapsing malaria were treated, 11 *P. vivax* and one mixed infection. They each received 8 intravenous injections of mapharside at intervals of six days, the first 0·04 and the remainder 0·06 gm. The results were good. A marked improvement in the general health of the patients and the reduction of the spleen to normal limits were noted. Only two patients had a further attack of fever during three months following treatment.

Eighteen chronic cases of malaria splenomegaly, 11 of them being afebrile, were treated with an association of typhoid-paratyphoid vaccine and mapharside. Six of the cases with very pronounced anaemia received preliminary treatment with liver extract and iron. One cc. of typhoid-paratyphoid vaccine was given weekly for eight weeks ; on the day following these injections, mapharside was given intravenously as in the acute malaria cases. In six cases the febrile reaction caused by the vaccine was very intense ; in these, subsequent doses of vaccine were lessened. There was marked improvement in the general health of all patients. The pain so commonly associated with great enlargement of the spleen disappeared after the first injections. There was noteworthy reduction in the size of the spleen in three cases ; slight reduction in two ; no apparent reduction in 10. Three patients did not complete the treatment.

Before using mapharside or any other trivalent arsenical a thorough examination of the patient is necessary to exclude contraindications to their use.

Norman White.

Unti, O. Dosagem da quinina e da quinidina no sangue. (Contribuição para a simplificação da técnica de extração e avaliação de alguns alcalóides da quina.) [**Estimation of the Quinine and Quinidine Content of the Blood : Contribution towards the Simplification of the Technique of Extracting and Estimating Cinchona Alkaloids.**] *Arquivos de Hig. e Saúde Pública.* São Paulo. 1944, Sept., v. 9, No. 22, 35–48. English summary.

Quinine, when treated with sulphuric, citric or tartaric acid, displays a blue fluorescence when exposed to the ultra-violet rays from a mercury vapour lamp with a special filter. This fluorescence disappears if hydrochloric acid be added to the solution. These facts are the bases of the author's method of estimating the quinine content of the blood, a method for which simplicity and accuracy are claimed. The method is described in detail.

One cc. of blood is mixed with 3 gm. of anhydrous sodium sulphate, triturated and transferred to a flask of 25 cc. capacity. The flask is placed in a water bath

and four or five drops of concentrated liquid ammonia are added to alkalinize the quinine salt. The alkaloid is extracted with 8 cc. of chloroform-ether, 8 parts of chloroform to two of ether in a water bath at 65°C. When the chloroform-ether is reduced to about one third of its volume it is cooled and decanted into another flask. Five cc. of chloroform-ether are then added to the residue in the first flask and the operation repeated, three times in all. The chloroform-ether from these three extractions is then evaporated to dryness. To the residue 2 per cent. sulphuric acid is added to make a solution of 1 cc., the volume of the blood used. The fluorescence exhibited by this solution when exposed to ultra-violet rays is compared with that given by solutions of quinine of known titre.

By this means quinine can be detected in blood when present in dilutions as great as one in 6,000,000. *Norman White.*

COGGESHALL, L. T., MARTIN, W. B. & BATES, R. D., Jr. **Sulfadiazine in Treatment of Relapsing Malarial Infections due to** *Plasmodium vivax*. *J. Amer. Med. Ass.* 1945, May 5, v. 128, No. 1, 7–8.

This report shows that sulphadiazine was of no value in preventing relapses in *P. vivax* malaria infections naturally acquired in the South-west Pacific area.

Thirty-three unselected patients suffering from relapsing *P. vivax* malaria were given antimalarial therapy, 30 with atabrine [mepacrine], 0·1 gm. thrice daily for seven days, and three with quinine. On the eighth day, sulphadiazine treatment was begun, 8 gm. on the first day and then 1 gm. every four hours night and day for a week. For a second week the dose of sulphadiazine was reduced to 1 gm. every six hours night and day. An attempt was made to maintain a blood level of 8 to 10 mgm. sulphadiazine per 100 cc. during the first week. There were no toxic manifestations other than mild microscopic haematuria in three patients"; this cleared after increase in the fluid intake, and alkalization of the urine. Within three months, 16 of these patients (48·5 per cent.) had had further relapses. The corresponding relapse rate of 134 patients who had had similar antimalarial treatment but without sulphadiazine was 46·2 per cent. The average blood concentration of sulphadiazine of the 16 patients who relapsed had been 7·7 mgm. per 100 cc.; that of the 17 patients who had not relapsed by the end of three months had been 7·6 mgm. per 100 cc.

Norman White.

COLLIGNON, E. La campagne antipaludique de 1943 dans le département d'Alger. [**The Anti-Malaria Campaign of 1943 in the Department of Algiers.**] *Arch. Inst. Pasteur d'Algérie*. 1944, June, v. 22, No. 2, 131–40.

The presence in the Department of Algiers of a large number of troops, most of whom were unprotected against malaria by previous exposure, obliged the antimalaria organization to concentrate all its resources on preventive measures throughout 1943. The usual epidemiological investigations had to be renounced. Fortunately the year was favourable. Deficient rainfall that had characterized the winter continued throughout the first half of 1943. The usual spring breeding places of anophelines were fewer and smaller than usual. The autumn rains were early, abundant and persistent and flushed many other habitual breeding places. *A. maculipennis* [probably *labranchiae*], the chief vector, was less in evidence than usual. During the summer in the mountains *A. bifurcatus* and *A. marteri* were found sharing common breeding places. With the assistance of the hydraulic services, extensive antilarval work was carried out. In spite of the presence of an abnormally large susceptible population and a shortage of antimalarial drugs, there were only localized outbreaks of malaria once summer

had set in, and these outbreaks were mostly quenched early in the autumn. The number of parasite carriers probably increased, however, owing to the insufficiency of drugs for adequate treatment, a fact which made the outlook for 1944 somewhat disquieting. *Norman White.*

SEELER, A. O. **The Inhibitory Effect of Pyridoxine on the Activity of Quinine and Atabrine against Avian Malaria.** *J. Nat. Malaria Soc.* Tallahassee, Fla. 1945, Mar., v. 4, No. 1, 13–19, 1 fig.

The fact that para-aminobenzoic acid, which is necessary for the growth of certain bacteria, inhibits the action of the sulphonamides is in support of WOOD's hypothesis that the sulphonamides act by displacing para-aminobenzoic acid, and thus depriving the bacteria of its use. On the assumption that drugs such as atebrin and quinine owe their antimalarial activity to the fact that they similarly displace some substance essential to the growth and survival of the parasites, the author decided to carry out tests on the effect of large doses of vitamins. In this paper he shows that pyridoxine administered orally or subcutaneously definitely inhibits the action of both quinine and atebrin on *Plasmodium lophurae* and *P. cathemerium* in Pekin ducklings and another unnamed avian parasite in some other host. The daily dose of pyridoxine was 500 mgm. per kgm. of bodyweight for oral administration and 200 mgm. when given subcutaneously. The drugs were administered into the crop in aqueous solution once daily. The degree of inhibition as judged by the percentage of infected erythrocytes on certain days varied with the dose of the drug. When the dose was the minimal effective dose, inhibition was practically complete, but with increasing dosage the inhibiting action of pyridoxine in the quantities employed became less marked. Thus with a dose of quinine of 10 mgm./kgm there was complete inhibition, whereas with a dose of 15 mgm./kgm. there was only a slight inhibitory action. It was thought that pyridoxine might influence the toxicity of quinine and atebrin. Experiment on mice showed, however, that the toxicity was in no way influenced even by the administration of massive doses of pyridoxine. How pyridoxine acts is unknown, for there is no information available as to whether this substance plays any part in the metabolism of avian malarial parasites. The author thinks it probable that both quinine and atebrin owe their antimalarial activity, at least to some extent, to their interaction with pyridoxine or a pyridoxine-like substance. [Compare the work by TRAGER, on biotin deficiency in relation to *P. lophurae* infections; this *Bulletin*, 1943, v. 40, 676, 825.] *C. M. Wenyon.*

COGGESHALL, L. T., PORTER, R. J. & LAIRD, R. L. **Prophylactic and Curative Effects of certain Sulfonamide Compounds on Exoerythrocytic Stages in *Plasmodium gallinaceum* Malaria.** *Proc. Soc. Exper. Biol. & Med.* 1944, Nov., v. 57, No. 2, 286–92.

Although quinine and atebrin are effective against blood forms of *P. gallinaceum* in chicks, they are inactive against exoerythrocytic stages of the parasite. According to KIKUTH & MUDROW [this *Bulletin*, 1940, v. 37, 188] plasmoquine has some effect against the latter. The study of drug action on exoerythrocytic forms offers some difficulty, since they are not numerous in the blood. A simple biopsy method allowing multiple examinations of brain tissue in each bird, without causing much damage, is described in this preliminary report. The developmental course of exoerythrocytic forms in treated and control birds can readily be followed. Recently an investigation of a similar nature has been reported by COATNEY & COOPER [this *Bulletin*, 1945, v. 42, 353]. White Rock chickens were inoculated with about 20,000 sporozoites obtained from

the salivary glands of infected *Aëdes aegypti* and suspended in 0·2 cc. of heparinized normal chick blood. For brain biopsy a small syringe of 0·25 cc. capacity, fitted with a 20-gauge needle and containing 0·02 cc. saline, was used. The needle was pushed into the brain cortex and rotated through a complete circle while applying slight suction, and by this means enough material for examination of a stained film was obtained. Following routine infection with sporozoites, the exoerythrocytic forms first appeared in brain capillaries 7–9 days after inoculation; the period was shortened by giving larger inocula. After inoculation of infected blood cells these forms appeared much later. Some spontaneous recoveries were noted by the above biopsy method after exoerythrocytic forms had appeared in the brain.

In one experiment, after the appearance of exoerythrocytic forms in the brain, following inoculation of infected blood, sulphaguanidine, sulphapyridine, sulphathiazole, sulphadiazine, sulphanilamide and quinine were given to the chicken host by mouth. Of a total of 13 birds which received the sulphonamide drugs in doses of 250–500 mgm. daily over a period of days, starting when exoerythrocytic forms were first seen, 10 recovered and three died; three others, which received 40 mgm. of quinine daily, also died. Each of four controls had exoerythrocytic forms in the brain; two died and two recovered. It was possible to pick out effective drugs early in treatment because of the altered appearance of the exoerythrocytic forms. When the experiment was repeated a number of times quinine and atebrin and many other compounds were found to be ineffective, while plasmoquine and 4 : 4′ diaminodiphenyl sulphone were only weakly effective. A number of drugs were also tested on sporozoite infections of the chicks. Sulphadiazine, alone or with quinine, prevented the appearance of exoerythrocytic forms. If drug treatment was withheld until after exoerythrocytic forms had appeared in the brain, sulphadiazine and sulphapyridine [sulphapyrazine is given in the table] destroyed them, while quinine and atebrin again proved inactive. *J. D. Fulton.*

BLACKWATER FEVER.

Birnbaum, D., Goldblum, N. & Kligler, I. I. **The Sensitivity of Malarial Blood to Hemolysis.** *Harefuah.* Jerusalem. 1945, May 15, v. 28, No. 10. [In Hebrew 213–17. [10 refs.] English summary 217.]

"1. The administration of quinine to healthy adults for seven days has no influence either on the red cell or reticulocyte counts or on the rate of hemolysis.

"2. The increased sensitivity of the erythrocytes to hemolyze in bile salts persists for about two months after the malarial attack.

"3. As to the hemolytic property of the drugs in the test tube, it was found that atabrine and sulfanilamide are not hemolytic; quinine and plasmochin are hemolytic only in high concentration. Quinine hemolyzes in a dilution of 1 : 900 and plasmochin in a dilution of 1 : 200.

"4. Quinine, atabrine and plasmochin together with bile salts cause hemolysis. Individually, in similar concentration neither the drugs nor the bile produced any hemolysis. Sulphanilamide did not influence hemolysis either in the test tube or when added to a solution of bile.

"5. The addition of 0·02 % $NaHCO_3$ to bile solution delays the hemolysis of normal and malarial blood by 1–1½ hours. The blood of patients with enlarged spleens is sensitive to hemolysis even in the absence of clinical symptoms and of organisms in the circulating blood.

" 6. $NaHCO_3$ delays hemolysis in quinine bile mixtures as well as in atabrin mixtures. A similar effect is produced by the addition of $KHCO_3$ or Na_2HPO_4.

" 7. The neutralization of quinine delays its hemolytic activity, but it seems that the hemolytic effect of a neutralized mixture of quinine and bile is greater than that of the individual substances in the same concentration. Acidity is an additional factor in producing hemolysis.

" 8. Serum-bile and serum-quinine-bile mixtures inhibit hemolysis. Our methods of examination revealed no difference between normal and malarial serum in respect to the hemolysis of erythrocytes. The sensitivity to hemolysis depends on the erythrocytes and not on the serum."

Swantz, H. E. & Bayliss, M. **Haemoglobinuria : Report of Ten Cases of its Occurrence in Negroes during Convalescence from Malaria.** *War Medicine.* Chicago. 1945, Feb., v. 7, No. 2, 104–7.

Among over 2,000 patients with malaria treated in an evacuation hospital in a forward area in a malarious island ten suffered from haemoglobinuria either during or shortly after treatment. All ten were Negroes, in spite of the fact that the majority of the malaria patients were of the Caucasian race. All recovered. All but one of the ten had previously had positive blood smears, but at the time of onset of the haemoglobinuria all blood smears were negative. The treatment of the malaria in most of these ten patients had been with quinine, quinacrine hydrochloride [mepacrine] and pamaquin naphthoate. The authors believe that pamaquin naphthoate may have played an important rôle in the production of haemoglobinuria in some of the cases ; it was not the only factor, for one patient had received none at all and in some others the onset of haemoglobinuria was delayed as long as three weeks after the discontinuance of the drug. It is curious that all the patients were Negroes ; the treatment of their malaria differed in no respect from that of other races. Most of the patients gave a history of having previously suffered from malaria in the southern United States. *Norman White.*

Singh, I. & Singh, I. **A Note on the Treatment of Black Water Fever with Antivenene.** *J. Indian Med. Ass.* 1945, Mar., v. 14, No. 6, 116–18.

Four patients with " blackwater fever " were treated with antivenene and recovered. A fifth, who did not receive antivenene, died. In the fatal case, anuria developed " which did not respond to medical methods." At autopsy the lower ends of both ureters were blocked with " a reddish brown clot." Three of the recovered patients had received pamaquin before " blackwater fever " developed ; the histories of the fourth case and the fatal case are not given.

The authors recommend surgical interference (either ureteric catheterization or unilateral nephrostomy) in anuric cases which do not respond to medical treatment.

[This paper is not very carefully presented and references to the literature are often misquoted and incomplete. For example, Ross (1942) is quoted as advocating pelvic lavage, but the reference is not given. The section of the paper devoted to the mechanism of anuria in blackwater fever has been written without reference to the literature apart from a quotation from the " Memoranda on Medical Diseases in the Tropical and Sub-tropical Areas, 1942," which, incidentally, is not placed in quotation marks, and is wrongly paged in the list of references. In the summary, the statement " a case of anuria was successfully

treated by ureteric catheterisation " has no connexion with the present paper, but apparently refers to a personal communication from Bingham (1944) mentioned in the text. The advice regarding surgical interference in blackwater fever is, in the opinion of the reviewer, thoroughly unsound.]

B. G. Maegraith.

TRYPANOSOMIASIS.

BAX, S. N. **Report on the Work of the Tanganyika Tsetse Research Department since February, 1944,** 12 pp., 2 charts. [Mimeographed report dated Shinyanga, 20th Nov., 1944.]

Various observations and experiments in the Field and laboratory have been continued during the past year and some new work carried out.

Tsetse in captivity.—JACKSON found that *G. morsitans* which were kept in darkness at outdoor temperatures and 100 per cent. relative humidity, synthesized less fat than was found in caught flies, and some died with full meals of undigested blood even three days after the meal. VANDERPLANK found that feeding with either sheep or fowl blood was suitable for reproduction and longevity in *G. morsitans* (Races A and B), *G. swynnertoni*, *G. pallidipes*, *G. austeni*, *G. palpalis fuscipes*, *G. palpalis martinii*, *G. longipennis*, *G. fuscipleuris*, and *G. brevipalpis*.

A tsetse feeding apparatus, designed by VANDERPLANK, in which rat skin-membrane, defibrinated blood, an electrical thermostatic heater, and a centrifugal pump are used, promises to save much time and to result in greater longevity and reproduction of the flies.

Field studies.—JACKSON found that inconspicuous (dark) colours gave no better survival in marked flies than conspicuous colours. VANDERPLANK continued experiments on scents; alcoholic extract of ox scent on screens doubled the catches of *G. pallidipes* and increased the catches of *G. swynnertoni* by 50 per cent. JACKSON confirmed MELLANBY's view [this *Bulletin*, 1937, v. 34, 558] that humidity does not affect the metabolism of fat; BUXTON and LEWIS [*ibid.*, 1935, v. 32, 369] and JACK [*ibid.*, 1940, v. 37, 400] got a contrary result. The amount of weight lost by a tsetse at 25°C. and 50 per cent. R.H. was found to be almost independent of its initial weight, hence small flies are at a disadvantage. Body weight is related to wing length. Age can be determined fairly well from the fraying of the wings.

GLASGOW investigated the process of deteneralization [cuticular hardening] in *G. morsitans* and concluded that the age of teneral [newly emerged] flies could be estimated by examination of sections of the cuticle, JACKSON studied the development of fat and the activity of tsetse.

When *G. morsitans* was introduced (as pupae) into a *G. swynnertoni* habitat, it produced a considerable second generation unless there was a great excess in numbers of *G. swynnertoni*, but the bodily condition of *G. morsitans* was not so good as in its own habitat. *G. palpalis* did fairly well in a riverine habitat in a *G. swynnertoni* area but failed completely away from the river; it seemed to feed on reptiles only.

Work on hybrids has been continued by VANDERPLANK; ten species—*G. morsitans* (Races A and B), *G. swynnertoni*, *G. pallidipes*, *G. austeni*, *G. palpalis fuscipes* and *martinii*, *G. longipennis*, *G. fuscipleuris*, and *G. brevipalpis*—and 1,200 tsetse, have been used [see also this *Bulletin*, 1945, v. 42, 99].

G. palpalis fuscipes and *G. palpalis martinii* mate at random but the male

martinii always kills the female *fuscipes* with its large superior claspers ; when the tips of the claspers were cut off, offspring were obtained. Some of the female offspring were fertile but the male offspring could not mate owing to abnormalities of the genital organs.

G. morsitans (Race B) from the Tanganyika coastal belt are genetically and morphologically different from the typical *G. morsitans* (Race A) of central Tanganyika ; male hybrids between these two races or subspecies are completely sterile, and the females are partly sterile when crossed back with either parent race. Race B crosses more readily with *G. swynnertoni* than with Race A and more offspring are produced ; male hybrids, however, are still sterile and females partly so.

G. austeni is generally prevented from mating with tsetse of the *morsitans* group owing to its size but insemination of females of that group by *G. austeni* males has taken place in the laboratory, but without offspring.

Other species mate outside their own species only very exceptionally.

Trypanosomes.—*T. congolense* has been shown by measurements to be dimorphic, and *T. rhodesiense* was found, by measurements in relation to its electric charge, to be tetramorphic, VANDERPLANK (below) has found an infection with *T. congolense* in a *G. austeni* female [in this report it is said to be a male].

In dissections of 30,000 wild *G. swynnertoni* and *G. pallidipes*, a seasonal variation in infection with trypanosomes was found ; it seems probable that a higher rate of infection occurs in the older, nonteneral flies. There has also been a steady annual fall in the infection rate during the last three years and a parallel seasonal and annual change in the incidence of trypanosomal infection in game animals was noted.

From a study of the nucleus of trypanosomes VANDERPLANK concluded that there were two sexes in all species so far examined, and he thinks that " sexual reproduction takes place by exchange of gametes in the fly. *T. brucei* has the same number of chromosomes as *T. rhodesiense* but in the former the Y chromosome is larger and more obvious. *T. simiae* is identical with *T. congolense*" [see also this *Bulletin*, 1944, v. 41, 829].

Further observations on the effects of fire-exclusion and clearing of the hard pans, and of selective clearing, were made at Shinyanga. As selective clearing failed to eliminate *G. swynnertoni* from experimental Block 7c, a hybrid experiment was made in June, 1944 ; about 144,000 *G. morsitans* (Race A) pupae from Kondoa Irangi were introduced into the area with the result that *G. morsitans* spread all over the area and outnumbered *G. swynnertoni* by 7 to 1 in September and October. Some hybrids have been caught in the block, but it is too soon to know whether the experiment will be successful in eliminating *G. swynnertoni*, though a considerable reduction in its numbers has occurred.

Further clearing has been done in *G. pallidipes* areas. *J. F. Corson.*

i. VANDERPLANK, F. L. **Infection of** *Glossina longipennis* **and** *G. fuscipleuris* **with** *Trypanosoma congolense*.. [Miscellanea.] *Ann. Trop. Med. & Parasit.* 1945, May 31, v. 39, No. 1, 61.

ii. ——. **A Note on Wild** *Glossina austeni* **Infective with** *Trypanosoma congolense*. [Miscellanea.] *Ibid.*, 62.

i. The author records that he succeeded in infecting both *Glossina longipennis* and *G. fuscipleuris* with *Trypanosoma congolense* by allowing them to feed on an infected sheep.

ii. Four species of *Glossina* occur at Kingolwira, near Morogoro, Tanganyika Territory ; in August, 1944, the author and a native assistant dissected nearly

a thousand wild tsetse and found a female *G. austeni* infected with *T. congolense*. The results of the dissections are shown in the following table:—

Species	No. dissected	Positive		Percentage positive	
		T. congolense	*T. vivax*	*T. congolense*	*T. vivax*
Male *G. morsitans*	679	34	14	5·0	2·1
Female ,,	123	5	1	4·1	0·8
Male *G. pallidipes*	38	0	0	—	—
Female ,,	28	0	0	—	—
Male *G. austeni*	17	0	0	—	—
Female ,,	17	1	0	(5·9)	—
Male and female *G. brevipalpis*	2	0	0	—	—
Total ...	904	40	15	4·4	1·7

Reference is made to the experimental transmission of *T. congolense* by *G. austeni* reported by Lewis, Wiley and Macaulay [this *Bulletin*, 1943, v. 40, 887]. *J. F. Corson.*

Calver, K. M. **Chemotherapeutic Studies on Experimental** *T. congolense* **Infections.** Thesis for degree of Ph.D., University of Glasgow. 1945. Unpublished; copies at University of Glasgow and Medical Research Council, London. 72 pp., 31 tables.

This is a detailed account of the effects of treatment of *Trypanosoma congolense* infections in mice by phenanthridinium compounds, reference being made also to the use of other drugs for these infections. There is also a considerable account of some of the immunity responses following cure, and finally recent reports of field trials of the phenanthridinium compounds No. 897 and No. 1553 are discussed in the light of the author's own work. The investigations, part of which have already been published in summary form [Browning and Calver, this *Bulletin*, 1945, v. 42, 259], were carried out under the guidance of Professor C. H. Browning (with the support of the Medical Research Council), and since the original report will not always be readily accessible, and since the introduction of the phenanthridinium drugs [Browning, Morgan, Robb and Walls, this *Bulletin*, 1938, v. 35, 344] constitutes an important advance in the control of trypanosomiasis of domestic stock, the thesis is here abstracted in some detail. It consists of an Introduction and seven Sections, each of which will be reviewed below, under the author's own headings.

Introduction.—This reviews briefly the history of the treatment of infections by *T. congolense*. Compounds such as trypanblue, trypaflavin, arsenicals, suramin styryl-314, etc., which have a favourable action on infections by other trypanosomes, have a poor effect on *T. congolense*, whilst tryparosan and bismuth salts have some therapeutic action, which, however, does not seem to be capable of practical application. The only compounds which have achieved any success in the field—and success of only very limited degree, prior to the introduction of the phenanthridinium series, are tartar emetic, and the German preparations, Antimosan and Surfen C.

Section I.—Experimental strains of T. congolense.—Two strains were used. Strain I, maintained continuously in mice since 1929, has been fully described by Browning, Cappell, and Gulbransen [this *Bulletin*, 1935, v. 32, 30];

Strain II, maintained also in mice since 1933, and more virulent to these animals than the other strain, was mentioned by P. Browning [this *Bulletin*, 1938, v. 35, 716].

Strain I reaches the "fastigium" or "acme," *i.e.* when parasites are uncountable in a microscope-field, about 7 or 8 days after inoculation; this stage is sometimes followed by the persistence of parasites in large numbers, with death in a few days, a so-called acute course, but more commonly, by either a relapsing course, with the first negative period occurring two to five days after the fastigium, or a chronic course in which the parasites never disappear from the blood, and may persist in considerable numbers, though fluctuating, for days or weeks. In order to retain unchanged the immunological character of the strain it is necessary to pass it on from mouse to mouse at the fastigium, and a line maintained in this way is referred to as the *acme strain of T. congolense I.* When the infection becomes relapsing-chronic, and parasites, after diminishing in the blood, again become numerous, this is referred to as a "relapse fastigium."

Strain II reaches the acme stage in about five or six days, after which, unlike Strain I, the parasites very rarely disappear or diminish to any great extent, and death supervenes from two days to several weeks later.

Section II.—Treatment of Experimental T. congolense Infection in Mice with No. 897.—This compound is 7 amino-9 (*p*-amino-phenyl) 10-methyl-phenanthridinium chloride [Morgan and Walls, *J. Chem. Soc.* 1938, 389], prepared at the Chemical Research Laboratory, Teddington. A dose of 1 mgm. per 20 gm. body weight is well tolerated by mice; 2 mgm. per 20 gm. is fatal in about 75 per cent. of cases. (Throughout, the drugs are given subcutaneously in a single dose, in a proportion of 1·0 cc. of aqueous solutions containing the amount stated per 20 gm. body weight.)

Strain I infections respond to treatment better than Strain II, about 60 per cent. of the former (treated at acme) being cured by a dosage of the order of 0·01 mgm, as against some 40 per cent. of the latter by a dosage of the order of 0·07–0·1 mgm. With both strains, treatment is substantially less effective if administered before the infections have reached the acme stage. This, together with the observation that trypanosomes usually persist, sometimes even increasing in numbers, for two to three days after treatment, is regarded as supporting the view that immunity reactions play a considerable part in the mechanism of cure; and it is in contrast to experience with the treatment of the very acute type of infection, *e.g.*, with *T. brucei*, where the infection becomes more difficult to cure as it progresses.

After non-curative treatment by No. 897, and 30 other phenanthridinium compounds tested, the duration of the parasite-free period, on blood examination was generally 9 to 14 days for Strain I, and 8 to 11 days for Strain II infections, the period being apparently independent of (*a*) the size of dose, (*b*) the stage of infection at the time of treatment, and (*c*) the particular compound used.

It was found that in the chronic stage, arbitrarily fixed at three to six weeks after the acme for Strain I and a few days after acme for Strain II, treatment is, as in the early stages, less effective than at acme. Such chronic infections are differentiated, under the designation of "chronic in the original mouse," from so-called "chronic strain" infections, defined as arising when the inoculum is derived from a mouse in which the infection has become chronic. It was a peculiar finding that as many as 28 per cent. of 149 mice failed to become infected after inoculation from animals chronically infected with Strain I. Inoculations from animals chronically infected with Strain II always produced infections.

In summary, the curability of various stages of infection in both Strains I and II, starting with the most readily cured, is as follows:—(*a*) acme, (*b*) early,

(*c*) a " chronic strain " infection treated at fastigium, and (*d*) the " chronic stage in the original mouse." These observations probably have an important bearing on the results under field conditions.

Prophylactic Action.—In contrast to the prolonged protective effect of Suramin and certain benzoylamino quinoline styryl compounds against *T. brucei* [BROWNING and GULBRANSEN, this *Bulletin*, 1935, v. 32, 28] No. 897 exercised only a slight prophylactic effect on *T. congolense*, a subcutaneous dose of 1 mgm. protecting against Strain I for two days, but not for a longer period.

Oral administration, in the form of daily feeding with bread soaked with 1 cc. of 1/1,000 solution, exerted neither prophylactic nor curative action.

Section III.—Treatment with other drugs.—A list is given of 46 substituted phenanthridinium compounds examined, all with a benzene ring in the 9-position. General conclusions about this series are as follows :—

The greatest activity against *T. congolense* is exerted by compounds with two amino substituents, situated either both in the phenanthrene nucleus or one in the latter and the other in the benzene nucleus. The actual position of these amino groups does not appear to influence activity, but two such groups in the benzene ring in the *m* positions are not associated with activity.

The activity of No. 897, which has an amino group in the phenanthrene and in the benzene nucleus, is impaired by the inclusion of a bromine atom in the 3– position.

A single amino group situated in either nucleus increases toxicity and reduces considerably the therapeutic action.

The acetylated derivatives are much better tolerated, but also much less active than the corresponding amino compounds.

An outstanding advantage of 1553 is its relative lack of the irritating effect on the tissues at the site of injection, exhibited by most of the other active compounds of this series.

The phenanthridines corresponding respectively to No. 897, and to one of the other active phenanthridinium compounds, were found to be inactive.

Diamidine series.—The compound 4 : 4′-diamidino dimethyl stilbene, considered by FULTON and YORKE [this *Bulletin*, 1943, v. 40, 19] to be at least as effective as No. 897 on their strain of *T. congolense*, was tested by the author. She found, however, that 1/75 of the tolerated dose of No. 897 has about the same curative action as 1/10 of the tolerated dose of the dimethyl stilbene drug, when tested on Strain I at acme. The latter compound appears, however, to be almost as effective in chronic infections as at acme, and it is therefore considered that a possible explanation of Fulton and Yorke's conclusion is that their observations were made on chronic infections.

Quindoline Methochloride (supplied by I.C.I.).—This compound is curative in doses approaching the maximum tolerated (1·3 mgm.), but the severe local reaction at site of injection renders it unsuitable for use. The corresponding hydrochloride is inactive.

Section IV. Treatment of Relapses.—In the case of Strain II, which was more exhaustively examined than Strain I under this head, relapsed infections were repeatedly treated by a uniform dose of 0·07 mgm. at each relapse. Fifty-six relapsed mice were thus investigated, the greatest number of relapses in any one animal being 29. Cure frequently resulted from these repeated treatments, and usually within six retreatments. The chance of cure by the standard dosage was the same in the treatment of relapses as in the treatment, at acme, of original infections (38 per cent.). This is contrary to the widely accepted belief, based on observations with infections by other trypanosome species, that cure is more certain by vigorous initial treatment, while cure of relapses presents special difficulties. An especially significant interpretation of these findings is that drug-resistance did not develop as a consequence of these

repeated retreatments. Only in two mice out of 47 which received three or more retreatments were there any indications of a slight resistance, in so far as relapses failed to respond to further treatment. This is elaborated under Section V.

In the case of Strain I infections, successive relapses were treated by 0·01 or 0·013 mgm. Unlike the experience above, relapses were, in general, not as easily cured as the original acme infections. In four mice out of six, definite indications of resistance appeared at the third to sixth treatment (in three weeks to two months). The dose was increased to 0·33 mgm. in two of these mice, and by the 12th treatment there was no response to this dose. However, infections derived from these two mice showed some response to 0·33 mgm., but in most the action disappeared after a few retreatments ; occasionally, after only slight responses to several consecutive treatments, subsequent treatments did produce a definite effect. On the whole, it was concluded that there was strong presumptive evidence that a true drug-resistance to No. 897 might be readily developed by this strain, but, as shown below, this proved to be extremely difficult.

Section V. Attempts to develop strains of T. congolense resistant to drug.

No. 897.—Strain I was passaged through 12 mice, in a period of six months, during which 20 doses were administered, rising from 0·013 mgm. to 0·1 mgm. The strain was then lost. It was considered that there had been no particular development of acquired drug-resistance in the ordinary sense, the apparent acquisition of the property being explained by the fact that in the course of the treatments a relapse (chronic) strain was developed, and such strains have been shown to be less responsive to treatment than the original strain treated at acme (see Section II).

Strain II was passaged through six repeatedly treated mice, which received altogether 39 doses of 0·07 mgm. and 26 of 0·33 mgm. In several instances, which occurred only in the earlier passages, there was some degree of resistance to 0·33 mgm. administered at acme, but in the subsequent passages this apparent resistance was no longer in evidence.

With both strains, further unsuccessful attempts to produce lasting resistance were made by the method designed to leave unimpaired the immunological and serological characters of the parent trypanosomes. This consists in treating the mice at a time when the infection is developing and the trypanosomes are scanty in the blood, with a dose which does not affect the course of infection ; the parasites are then transferred at acme to a fresh host. With Strain I the attempt involved 16 passages, over a period of four months, during which the dose was increased from 0·005 mgm. to 0·02 mgm. With Strain II there were 34 passages in 8 months, with doses from 0·0013 mgm. to 0·017 mgm.

It was concluded from all this work that true lasting drug-resistant strains of *T. congolense* had not been produced, and are not easy to produce, by these standard methods, which are so effective in bringing about resistance to other drugs in other trypanosomes, such as *T. brucei*.

Section VI. Immunity Responses after Cure.—This was investigated in considerable detail, with very interesting results, which cannot all be summarized in a few lines.

With Strain I there is a remarkably solid immunity to reinoculation with homologous acme trypanosomes, lasting at least 13 months, in mice cured either at acme or in the chronic stage. There is however, with very rare exceptions, no immunity in such mice to reinoculation with random strains of chronic trypanosomes, even if the reinoculation be from the same animal as yielded the original infection.

The results of a considerable number of immunity tests led to the general interpretation that the immunological characters of the trypanosomes undergo progressive change in chronic infections. However, by passage of a chronic

infection to a fresh mouse, from which the subsequent transfers are made only at the fastigium, the immunological character of the chronic strain may, for a time, be preserved ; but after a very variable number of such transfers (less than three or more than 12) the immunological character tends eventually to revert to that of the " acme " parent type.

Chronic strains are evidently immunologically heterogeneous. Expressed in terms of Ehrlich's receptor theory, when an infection of the " acme strain " is allowed to become chronic, additional receptors appear, but do not replace the original A type. The receptors may be regarded as becoming progressively A+B, A+B+C, etc., which on cure gave rise to anti- (A+B), anti- (A+B+C), etc. Thus a mouse whose immunity depended on anti- (A+B) would be immune to trypanosomes with receptors A or A+B (or B), but not to those which contained additional receptors, as in A+B+C. The effect of further fastigial passages is to prevent development and accumulation of additional receptors and eventually to lead to their disappearance.

With Strain II, in contrast to Strain I, mice cured at acme do not manifest a 100 per cent. immunity to reinoculation by homologous acme trypanosomes. The chances of such a reinoculation resulting in infection are about 50 per cent., and bear no relation to the size of dose used to effect cure, or to the duration of the period which has elapsed since cure (up to the limit tested, 8 months). Where reinfection does eventuate, the incubation period is nearly always about four days longer than in controls, this being interpreted by the author as indicating a slight degree of resistance to the homologous strain.

A number of animals which had proved immune were repeatedly reinoculated with acme trypanosomes, but the chances of infection remained about 50 per cent., at least for the first few reinoculations, with perhaps a tendency to a higher proportion of immunes as the number of reinoculations increased. In similar experiments with Strain I it had been found that cured mice originally infected with acme trypanosomes withstood up to 20 homologous reinoculations.

Cured chronically infected Strain II mice responded to reinoculation with acme parasites in the same manner as cured acme animals (50 per cent. likelihood of immunity), but no immunity was observed in cured acme mice on reinoculation with random chronic parasites. This corresponds with findings in similar experiments with Strain I, and it was tentatively concluded that when a Strain II infection becomes chronic, the trypanosomes undergo the same kind of mmunological changes as those of Strain I, *i.e.*, there is an addition to, but no replacement of, the original receptors.

There is no cross-immunity between the two strains, animals cured at acme after infection with acme trypanosomes of Strain I becoming infected on reinoculation with acme parasites of Strain II, and *vice versa*. There was, however, some indication that a history of a cured Strain I infection improves a mouse's chances of developing an immunity to Strain II, on cure of a subsequent infection by the latter strain.

Attempts to apply the adhesion reaction of Rieckenberg [this *Bulletin*, 1917, v. 10, 56], with a view to detecting immunological differences or identities among the various strains, were unsuccessful.

Section VII. Field Trials of No. 897 and No. 1553 on T. congolense Infections. These have been as follows :—

No. 897.—Hornby, Evans and Wilde (*J. Comp. Path.*, 1943, v. 53, 269), Carmichael and Bell, 1944 (1) [this *Bulletin*, 1945, v. 42, 259], unpublished communications of du Toit to the National Institute for Medical Research, 1941, and by Marshall to the Department of Scientific and Industrial Research, 1943.

No. 1553.—Carmichael and Bell, 1944, (2) [this *Bulletin*, 1945, v. 42, 260]. The author's own results are considered in relation to field trials, with the following conclusions :—

(1) Favourable reports have appeared from widely separated localities, in Tanganyika, Uganda and Nigeria, although very considerable variation in the tractability of infections in the field might be expected, in view of the fact that the two laboratory strains here described have been shown to differ so much in their reactions to treatment, and in related properties.

(2) The stage of infection at the time of treatment should be noted, in reports of field trials, since this has been shown in mice to be of considerable significance.

(3) The difficulty of producing a drug-resistant strain under experimental conditions indicates that No. 897 is a valuable drug for use in the field. The resistance reported in relapsed infections [Hornby, *et al.*, 1943, *loc. cit.*; Carmichael and Bell, 1944, (1), *loc. cit.*] is probably attributable to the chronicity of the infection rather than to true acquired drug resistance. Thus, in the present work, the curative dose for a chronic infection may be at least 5 to 10 times that required at acme.

(4) The fact that, with one of her strains, cure at acme is followed by a solid immunity, suggests to the author that if such a solid immunity can be demonstrated in the field it may be utilized to protect animals passing through fly belts, by previously infecting and then curing them. [But natural transmission in the field is very different from blood inoculation of a fastigially propagated strain, and it was only to such inoculations that a solid immunity was demonstrated.] From results obtained with the other strain, however, the author considers that such protection would not be expected with all strains, under field conditions.

(5) The author showed that in mice a greater degree of immunity was manifested to laboratory Strain II parasites in the presence of antibodies to Strain I than in animals which had never been infected with the latter. Accordingly, it is suggested that a more solid immunity might follow cure of a mixed infection with several strains of *T. congolense* than would occur after infection with a single strain. *E. M. Lourie.*

Walls, L. P. with a note by C. H. Browning, K. M. Calver & M. W. Leckie. **Researches in the Phenanthridine Series. Part VI. The Relationship between Structure and Trypanocidal Properties.** *J. Chem. Soc.* 1945, May, 294–300.

" Certain amino-substituted quaternary salts of this series possess trypanocidal properties, and the effect of variation in number and position of the substituents has been investigated. An improvement has been effected in the method of ring closure of acyl-*o*-xenylamines (I→II), and it has been found that the facile preparation of nitro-quaternary salts such as 2 : 7-dinitro-9-phenyl-10-methylphenanthridinium chloride (IV ; R=R′=NO_2, R″=H) followed by reduction, offers an alternative and generally preferable route to the trypanocidal types. In order to obtain a similar bromo-substituted compound it has been shown that bromination of 4′-nitro-2-acetamidodiphenyl occurs as expected in the 5-position.

" Activity against *T. congolense* is well maintained in all the diamino-quaternary salts except when both amino-substituents are in the 9-phenyl group. Pronounced action against *T. brucei* is only found in (IV ; R=R′=NH_2, R″=H), where the amino-groups are in the ' benzidine ' position. Acetylation of the amino-groups results always in diminution in activity."

UNDERWOOD, L. J. **Nitritoid Reaction following Tryparsamide Therapy : Report of a Case.** *Arch. Dermat. & Syph.* 1945, May, v. 51, No. 5, 313–15. [13 refs.]

BRAZZAVILLE [A. E. F.] : RAPPORT SUR LE FONCTIONNEMENT TECHNIQUE DE L'INSTITUT PASTEUR EN 1943 [CECCALDI, J., Director]. 59–85. Surveillance de la maladie du sommeil. [**Sleeping Sickness.**]

Two European missionaries, infected at the same time and place, were treated at the Pasteur Institute at Brazzaville during 1943 ; each received about 11 injections of about 1 gm. of moranyl [Bayer 205] during about two months. Both were in the early stage and recovered.

There were 165 new cases among Africans, coming from various parts of the territory ; they were treated with the usual drugs, given either alone or in combination. Orsanine (270 F.) was considered to be the most effective drug used.

Four hundred and ninety old cases were examined ; 27 had been diagnosed between 1918 and 1928 (three still infected) and 141 between 1928 and 1938 (14 still infected).

Tests of toxicity of old stocks of atoxyl or trypoxyl, tryparsamide, and orsanine were made on rabbits, rats and mice ; atoxyl had altered and was rejected, orsanine had preserved its normal characters, and tryparsamide of French manufacture, though slightly altered, was more satisfactory than supplies of more recent date of American (SQUIBB) manufacture.

Some observations are given which strongly suggested that reinfection had occurred in some patients after cure. *J. F. Corson.*

WOOD, S. F. **Additional Notes on the Persistence of *Trypanosoma cruzi* in Dead Insect Vectors.** *Bull. S. Calif. Acad. Sci.* Los Angeles, Calif. 1944, v. 42, Pt. 3, 115–27. [Summary taken from *Rev. Applied Entom.* Ser. B. 1945, May, v. 33, Pt. 5, 72–3.]

Details are given of experiments on the persistence of various strains of *Trypanosoma cruzi* in a viable state in nymphs of *Triatoma* spp. after they had died naturally in the laboratory or had been killed or immobilised by exposure to hydrocyanic acid gas. Some treated with the gas survived for many days and could, if stimulated, move legs and antennae, but could not crawl. The longest periods for detection of living stages of the trypanosome after natural death of the bugs were 41 days in *T. protracta*, Uhl., three days in *T. protracta woodi*, Usinger, and 24 days in *T. rubida*, Uhl., and the longest periods after death or immobilisation by cyanide were 127 days in *T. protracta*, 122 days in *T. rubida* and 16 days in *T. longipes*, Barber. The author considers that the persistence of *Trypanosoma cruzi* in dead bugs is of importance in maintaining a large rodent reservoir of infection, since rodents acquire infection by feeding on them. They would be particularly likely to notice dying bugs that still moved their antennae or legs.

Some of the bugs in all the cultures used for these experiments were found to be infested by *Ereynetes concolor*, Hald. This mite occurred most often on *Triatoma rubida* from nests of wood rats [*Neotoma*] in Arizona. No trypanosomes were found in mites from infected bugs.

WOOD, S. F. **Observations on Vectors of Chagas' Disease in the United States. I. California.** *Bull. S. Calif. Acad. Sci.* Los Angeles, Calif. 1942, v. 41, Pt. 2, 61–9. [22 refs.] [Summary taken from *Rev. Applied Entom.* Ser. B. 1945, May, v. 33, Pt. 5, 72.]

This is the first part of a series of which the second has already been noticed. It includes a review of the papers in which *Trypanosoma cruzi* has been recorded

in Triatomids in California, Arizona, Texas and New Mexico ; a list of the species examined for infection in these States and (with negative results) in Utah, showing the numbers of each and the numbers and percentages infected ; new locality records for infection in *Triatoma protracta*, Uhl., in California ; lists of numerous Californian mammals in which infection was not found by blood examination or xenodiagnosis ; and a discussion of the effects of the bites of Triatomids on man, which are severe in some individuals and imperceptible in others. In California, *Trypanosoma cruzi* has been found only in *Triatoma protracta*, in a single example of *Neotoma fuscipes macrotis* and, possibly, in a bat.

Dao, L. Luis. Muertes subitas en la enfermedad de Chagas. [**Sudden Death in Chagas's Disease.**] *Bol. de los Hospitales.* Caracas. 1944, Nov.–Dec., v. 43, No. 6, 303–11. [14 refs.] English summary (9 lines).

Two cases are recorded, both in men—one aged 39 years, the age of the other is not known. The former applied for treatment on account of fever, shivering, sweating and a general " tired feeling." His heart was enlarged and its action irregular. *P. vivax* in scarce numbers was found in his blood, but no trypanosomes. The xenodiagnostic test was, however, positive. He was treated for the malaria and the fever disappeared. Eight months later he suddenly fell dead.

The second patient complained of palpitation, which was aggravated on slight exertion. His heart was enlarged, as was also the liver ; faecal examination revealed a few ova of *Necator americanus*. Xenodiagnosis was positive in this case also. About 12 weeks later, after a day or two of fever which disappeared without treatment, the man was one morning found dead in bed.

The author discusses the possible, or rather the probable, causes of sudden death. He excludes syphilis by the negative Kahn reaction in each case ; there were no schistosomes to account for the myocarditis ; hookworms were absent from the first and only scarce in the second patient, whereas the positive results of the xenodiagnostic tests proved the existence of Chagas's disease. The diffuse myocarditis, separation, fragmentation and hyaline degeneration of the myocardial fibres are well known in chronic cases of this disease and would readily account for these sudden deaths. Incidentally they add further evidence of the presence of this disease in the State of Anzoátegui, Venezuela. The author refers to the literature for preceding accounts of sudden deaths of young adults in endemic centres of Chagas's disease. *H. Harold Scott.*

LEISHMANIASIS.

Lowe, J. **The Early Diagnosis of Kala-Azar.** *Indian Med. Gaz.* 1944, Oct., v. 79, No. 10, 459–65, 3 figs.

The importance of the early diagnosis of kala azar is illustrated by the detailed description of five cases in which the most constant finding was the irregularity of the temperature, of remittent nature, with a relatively rapid pulse and the absence of the marked toxaemia of enteric fever or the headache and pains in the back and limbs so frequently met with in malaria. The absence of toxic symptoms accompanying the early fever is characteristic of kala azar. The only other early findings are a positive complement fixation and the presence of leishmania in sternal puncture material. The complement fixation test is carried out with the WKK antigen prepared from acid-fast bacilli. As regards the discovery of leishmania, a search of an hour may be necessary before a parasite can be found in the smears. In early cases all the characteristic

features, including the serological and blood changes of well developed kala azar, are absent, so that diagnosis may be difficult. Nevertheless, by careful observation of the general clinical picture and the nature of the fever, combined with sternal puncture and the complement fixation test, which is often positive in early cases, diagnosis should usually be possible within three weeks of onset. One condition, however, is essential, namely that kala azar should be thought of and considered as a possible diagnosis. *C. M. Wenyon.*

STEWART, C. D. & PILCHER, J. F. **American Leishmaniasis : Report of an Autochthonous Case.** *Arch. Dermat. & Syph.* 1945, Feb., v. 51, No. 2, 124–8, 2 figs. [Refs. in footnotes.]

American leishmaniasis (muco-cutaneous leishmaniasis), a common disease in S. America, is of rare occurrence in the United States. Only three cases have been reported in the literature, and of these only one has been regarded as autochthonous. This was a case reported by BENEDEK [this *Bulletin*, 1940, v. 37, 778]. FOX (*Arch. Dermat. & Syph.*, 1941, v. 43, 1093), however, expressed a doubt, as the patient had spent four years in Poland fifteen years prior to the development of mucocutaneous lesions of the nose. Fox stated that if the disease were really American leishmaniasis it must have been contracted in Poland [a conclusion which seems unjustifiable, as no form of leishmaniasis has ever been reported from that country]. However this may be, there appears to be considerable doubt about the diagnosis in Benedek's case, as pointed out by the reviewer. The case reported in the present paper was in a boy six years of age who had never been more than 60 miles from his birthplace near Alice in Texas. He first developed a papule on the dorsum of the left foot. This gradually enlarged and ulcerated, while similar papules and ulcers developed on the right foot, knee and buttock. There were few subjective symptoms, though a generalized lymphadenopathy was noted. In sections of tissue removed from the ulcer on the right foot, bodies were seen within cells or free in the tissue spaces. These were identified as leishmania by the authors and other observers. About a year later the cutaneous lesions had healed, but superficial ulceration on both sides of the anterior part of the nasal septum was discovered. The generalized lymphadenopathy persisted. In spite of the fact that leishmania were not found in the nasal ulcers, the authors state that they have no doubt that the nasal lesions represent the beginning of the tertiary stage of American leishmaniasis. [It is unfortunate that leishmania were not found in Giemsa-stained smears of any of the lesions, for the identification of these parasites in sections is always open to question unless made by an observer who has had extensive experience of these particular organisms. The microphotograph illustrating the paper is a good one, but though suggestive of leishmania, it is not absolutely convincing.] *C. M. Wenyon.*

PESSÔA, S. B. & VILLELA, F. Nota sôbre tratamento da leishmaniose tegumentar americana pelo antimon-detoxin. [**Treatment of Cutaneous and Muco-cutaneous Leishmaniasis with "Antimon-ditoxin".**] *Brasil-Medico.* 1944, Nov. 18 & 25, v. 58, Nos. 47 & 48, 442–3.

The authors give an account of their experience in the treatment of cutaneous and muco-cutaneous leishmaniasis with "antimon-ditoxin." This is a preparation issued by Wülfing of Berlin. It is similar to "auro-ditoxin" and is put up in ampoules to be dissolved in the solvent supplied. The makers advise the administration by intramuscular injection, a dose to be given every two days, commencing with 0·05 gramme. The second and third doses are 0·1 and 0·2 gm., respectively. The 0·2 dose is continued for a further 8 or 10 injections. The

authors found that in this dosage there were no signs of toxicity, so in some cases they continued the 0·2 gm. dose for 30 injections. In certain resistant cases 0·3 gm. was used. It was evident that the drug had a curative action on several cases of naso-pharyngeal involvement, some of which cleared up entirely. Though the drug is evidently superior to tartar emetic and Fouadin, some relapses occurred. In view of its low toxicity the authors propose using the still larger doses of 0·3 to 0·5 gramme. *C. M. Wenyon.*

FEVERS OF THE TYPHUS GROUP.

Blanc, G.; Martin, L. A.; Baltazard, M. Etude du comportement des virus exanthématiques chez divers ectoparasites. [**Study of the Behaviour of the Typhus Rickettsiae in various Ectoparasites.**] I. Comportement du virus du typhus murin chez le pou de l'âne, *Haematopinus asini* [Blanc, Martin & Baltazard]. *Arch. Inst. Pasteur du Maroc.* 1944, Oct., v. 2, No. 4, 578–85. II. Comportement du virus du typhus épidémique chez les puces, *Xenopsylla cheopis* et *Pulex irritans* [Blanc & Baltazard]. *Ibid.* 586–601. III. Comportement des virus de la fièvre boutonneuse et de la fièvre pourprée chez les puces, *Xenopsylla cheopis* et *Ctenocephalus canis* [Blanc & Baltazard]. *Ibid.* 602–10. [Bibliography.]

In the experimental work dealt with in this abstract an insect is regarded as being a potential vector when the following conditions are complied with :— (1) The insect is infected by a single meal. (2) The insect should remain infected for life. (3) The virus should multiply in the body of the insect. (4) The virus must be demonstrable in the faeces of the insect and must survive in the dried faeces.

I. Behaviour of Murine-Typhus Rickettsiae in the Ass-Louse *Haematopinus asini* [see this *Bulletin*, 1940, v. 37, 262].

The above conditions were fulfilled in the case of lice collected from two asses which had received massive intravenous injections of murine rickettsiae. The lice were first found infected 10 days after the inoculation of the hosts; lice collected during the febrile stage of the illness of the asses were not infected.

II. Behaviour of Epidemic-Typhus Rickettsiae in the Fleas *Xenopsylla cheopis* and *Pulex irritans*.

X. cheopis fed on a single occasion on guineapigs infected with epidemic typhus also complied with the above conditions; they remained infected for the rest of their lives, which were not shortened by the infection. Further experiments confirmed the findings of Dyer and others that the flea does not transmit infection by its bite. Three out of five monkeys became infected after the application of infected flea faeces to the conjunctiva or to the nasal and buccal mucosae.

P. irritans also complied with the prescribed conditions and can be regarded as a potential vector of epidemic typhus, but it is difficult to rear and does not feed readily on guineapigs.

III. Behaviour of the Rickettsiae of Boutonneuse Fever and Rocky Mountain Spotted Fever in *Xenopsylla cheopis* and *Ctenocephalus canis*.

By a series of experiments in which white rats and guineapigs were used it was found that the rickettsiae of boutonneuse and Rocky Mountain fevers survived in the bodies of the above fleas but did not multiply in them and were not passed out in the faeces. This is a new observation; the other two—I and II—have already been published. *John W. D. Megaw.*

Blanc, G. & Baltazard, M. Recherches sur l'immunité dans les maladies exanthématiques humaines. [**Investigations into the Immunity conferred by Human Typhus Fevers.**] I. Immunité conférée par l'infection apparente. *Arch. Inst. Pasteur du Maroc.* 1944, Oct., v. 2, No. 4, 611–24. II. Immunité conférée par l'infection "inapparente" ou l'infection "atténuée." *Ibid.* 625–32. III. Qualité de l'immunité. "Réinfection inapparente." *Ibid.* 633–50. IV. Immunité générale et immunité locale. *Ibid.* 651–5. [Bibliography.]

The work described in this memoir was carried out in Morocco between 1933 and 1942; some of the findings have already been published.

I. Immunity Conferred by Apparent Infection.

Experiments were carried out in which five strains of murine rickettsiae, seven strains of epidemic, nine strains of boutonneuse, and one strain of Rocky Mountain spotted fever rickettsiae were used. In the course of the investigation 683 guineapigs, 91 human beings, and 36 monkeys were employed.

It was found that a frank attack either of murine or epidemic typhus caused complete and lasting immunity against both murine and epidemic infection. In the case of one human being the immunity was tested after 5½ years.

A corresponding degree of immunity was conferred against both boutonneuse and Rocky-Mountain infection by a frank attack of either of these diseases.

All the strains of each of the rickettsiae were found to be identical in their pathogenic and antigenic powers, and, especially in the case of murine typhus, there was no difference in virulence or immunizing powers, although the strains came from three different countries and included one from Mexico.

II. Immunity Conferred by "Inapparent" or "Attenuated" infection.

In a large series of experiments it was found that certain animals and human beings which had shown no obvious reaction to a virulent experimental infection were afterwards (up to five years in one case) found resistant to massive doses of infection, and so could be assumed to have had an inapparent infection in the first instance.

Just as bile-treated living vaccine made from endemic typhus rickettsiae protects against both endemic and epidemic infection, so also living vaccine prepared from boutonneuse rickettsiae was found to protect 34 guineapigs and four monkeys against both boutonneuse fever and Rocky Mountain spotted fever, although the response to the vaccine in the case of the guineapigs had been inapparent and in the case of the monkeys had been attenuated. The authors insist that the only proof of the occurrence of an inapparent infection is the production of immunity against the organism concerned; when this immunity does not develop the inoculation must be regarded as having failed. The occurrence of a slight febrile response is not evidence that infection has occurred; workers with murine and boutonneuse rickettsiae know from experience that the result of intraperitoneal inoculation of guineapigs nearly always is either apparent infection or a failure to infect; they also know that the recovery of the rickettsiae from the blood of the animals is very difficult even when the infection is intense, when the infection is inapparent it is almost impossible. The authors have, however, succeeded in isolating the virus from guineapigs inoculated intradermally with bile-treated murine vaccine; the method was one of xenodiagnosis; the infected animals were kept in a receptacle containing large numbers of laboratory-bred fleas, from which suspensions were made after 30 days. They conclude that when a person or animal is found susceptible after inoculation with attenuated live rickettsiae, there must have been a failure to produce infection.

III. The Quality of the Immunity, "Inapparent Reinfection."

Numerous attempts were made to demonstrate the occurrence of inapparent reinfection in animals that had recovered from attacks of murine, epidemic,

and Rocky Mountain fever, dating from one and a half to seventeen months previous to the experiments. Out of a very large series, success was obtained in only one case in which a guineapig became infected with Rocky Mountain spotted fever 14½ months after recovery from an inapparent attack of boutonneuse fever. Inapparent reinfection must, therefore, be very rare, and animal reservoirs of infection must be infective to the vectors only during the brief periods while they are suffering from their first attacks.

In the tick-borne typhus fevers, hereditary transmission in the ticks [transmission through the egg would be a more accurate expression] readily explains the persistence of infection, but in murine and epidemic typhus another explanation must be sought.

IV. General and Local Immunity.

Various experiments, hitherto unpublished, are described, which confirm the observations by GIROUD and the authors that the sites of intradermal and intraorbital inoculations with typhus rickettsiae are less sensitive to reinoculations than other corresponding sites. *John W. D. Megaw.*

BLANC, G. E. BALTAZARD, M. Recherches sur le mode de transmission du typhus. [**Investigation of the Mode of Transmission of Typhus Fever.**] I. Non-transmission du typhus exanthématique par piqûres de poux infectés. *Arch. Inst. Pasteur du Maroc.* 1944, Oct., v. 2, No. 4, 656–7. II. Le réservoir de virus naturel des typhus, les déjections d'ectoparasites infectés. *Ibid.* 658–73. [Bibliography.]

I. Non-transmission of Typhus Fever by the Bites of Infected Lice.

This note has already been published (*Bull. Acad. Méd.*, 1942, v. 126, 444) under the same title.

Eight human volunteers were bitten by a large number (about 140 each) of infected lice kept in a tube whose mouth, covered by bolting silk, was kept upwards while the lice were feeding, so that there was no possibility of contamination of the skin by the droppings of the insects. No infection resulted: the lice were later proved to be infected, and the volunteers were afterwards shown to be susceptible to murine typhus.

II. The Natural Reservoir of the Typhus Rickettsiae is infected Faeces of the Ectoparasites.

In this paper the authors have brought together the reports of various investigations already published by them in separate papers from 1937 to 1942.

The method of collecting the faeces of infected fleas is described. Stress is laid on the uniform virulence and the indefinitely prolonged keeping properties of the dry faeces. *John W. D. Megaw.*

BLANC, G. & BALTAZARD, M. Transmission et conservation naturelles des typhus. Immunité. Epidémiologie. Prophylaxie. **[The Natural Transmission and Maintenance of Infection of the Typhus Fevers. Immunity. Epidemiology. Prophylaxis.]** *Arch. Inst. Pasteur du Maroc.* 1944, Oct., v. 2, No. 4, 674–715. [157 refs.] [Bibliography.]

In this note, hitherto unpublished, the authors discuss the subjects mentioned in the title. They again insist that none of the typhus rickettsiae can undergo mutation by passage through invertebrate vectors, although the rickettsiae form groups, the members of each of which show a considerable range of adaptability to different vectors. The groups recognized by the authors are (*a*) epidemic and murine rickettsiae, each of which is experimentally transmissible both by various lice and various fleas, and (*b*) the tick-borne typhus rickettsiae, each of which is transmissible by a considerable number of species of ixodid ticks. The rickettsiae belonging to each of these groups are not transmissible

by the vectors which transmit those of the other group. The authors, surprisingly, state that the various rickettsiae of the "river fever in the East Indies, China, and Japan," ought to be included among the rickettsiae of the tick-borne group. This is the only mention that is made of mite-borne typhus fever.

The authors admit that murine rickettsiae may exceptionally be transmitted in natural conditions from man to man by lice and so give rise to small human epidemics, but they argue that if this should ever happen it could only be in louse-infested communities, and that a benign infection would be caused which would help to stamp out epidemic typhus in the affected area. In a chronological review of the question of transmission, the authors in the same number of the *Archives de l'Insitut Pasteur du Maroc* state that the mystery of "tabardillo" in Mexico has arisen because of the coexistence of murine and epidemic rickettsiae in the same locality, and that, contrary to an erroneous statement made by themselves, there is no evidence that the human louse has ever been found naturally infected by murine strains.

In discussing the maintenance of typhus infection during inter-epidemic periods, the authors refuse to admit that inapparent attacks play any important part, though during actual epidemics such attacks help to maintain infection among lice. Occasional sporadic attacks during inter-epidemic periods are believed to be caused by dried infected faeces adhering to the clothing of persons who have been attacked during epidemics. The sporadic attacks are not usually highly infectious, but for unexplained reasons one of them may be highly virulent and so give rise to a fresh epidemic. Infected faeces of lice are quickly inactivated by moisture, so that the mere washing of patients' clothing is a valuable measure of control; sterilization of the clothing by steam under pressure, is, however, more reliable because it destroys the lice as well as the rickettsiae. Louse control, by itself, is inadequate.

The nature of the immunity in typhus fevers is discussed at some length; the authors assume that so long as antibodies can be detected in the serum the rickettsiae still persist in the internal organs and immunity remains complete; this condition may last for several years. After the disappearance of the antibodies and the rickettsiae, immunity becomes partial so that inapparent attacks may occur. The authors also believe that attacks may occur in which the endothelial cells are not invaded, so that the infection is purely humoral; this condition may exist in healthy carriers of infection and in inapparent reinfections, and it would not give rise to lasting immunity such as is produced by the presence of the rickettsiae in the cells. The immunity produced by killed vaccines is believed to be of this humoral, and therefore short-lived, type.

[It has been possible to mention only a few of the findings and expressions of opinion recorded by the authors in the collected papers dealt with in this and the three preceding abstracts. These papers constitute a comprehensive report of the vast amount of experimental work carried out by them during the past few years.

In a preliminary paper the authors present a historical review of research into the transmission of the typhus fevers, and they also append a useful bibliography containing 157 references.] *John W. D. Megaw.*

CASTAÑEDA, M. Ruiz. **Differentiation of Typhus Strains by Slide-Agglutinative Tests.** *J. Immunology.* 1945, Mar., v. 50, No. 3, 179–83.

A rickettsia-agglutination slide test has been used by the author to show that antigenic differences exist between classic and murine typhus. The rickettsia suspensions were made from the lungs of mice infected intranasally by murine and classic strains and were standardized by slide-agglutination tests of sera of guineapigs or rabbits convalescent from murine and classic

infections. Equal drops of the suspensions and of sera diluted 1–5 to 1–80 were mixed on the slides, which were kept in gentle movement; the readings were made after 1–3 minutes with a pocket lens. In all the examples given in the paper the agglutinations with the homologous sera were always at titres at least four times as high as those with the heterologous sera.

In applying the test to human sera, dilutions ranging from 1–20 to 1–640 were used; inactivation of the serum did not affect the result. A loop of 4 mm. outside diameter was made with No. 24 wire; with this, single drops of diluted sera and of suspensions were mixed on the slides, which were placed in large Petri dishes, each containing a piece of wet cotton, and kept moving for 5–10 minutes.

In a table the results obtained by complement-fixation and slide test applied to the same sera are compared. In the following three examples the first serum was from a patient convalescent from proved murine typhus, the other two were from patients living in an area where only murine typhus had been known to occur.

Day of Disease	Weil-Felix titre	Complement-fixation titre		Slide-agglutination titre	
		Classic	Murine	Classic	Murine
Convalescence	640	20	160	160	1,280
12th	640	160	640	40	160
12th	640	0	160	80	640

The Weil-Felix titres shown above were the highest tested.

In most of the other 10 cases, in which the identification of the type of the disease was based solely on the tests, the responses were equally clear-cut, but in one of the sera the complement-fixation titre was the same (1–320) with both murine and classic antigen, whereas in the slide test the titre with murine rickettsiae was 1–160 and that with classic rickettsiae was 1–640. In another case the titres of both tests were only twice as high with classic antigens as with murine. In still another case there was a great discrepancy between the results with the two tests, the fixation titre was 1–160 with classic antigen and 0 with murine, yet the corresponding titres with the slide test were 1–320 and 1–160.

There were altogether four cases among the 13 in the present series in which the agglutination titres with the presumably homologous human sera were only twice as high as those with the presumably heterologous sera, and some serologists are likely to doubt whether this difference is significant in a test of this kind. With the complement-fixation test the differences in titre were much more pronounced, though, exceptionally, in one case the titres with classic and murine antigen were the same and in another the classic titre was 1–160 and the murine 1–80.

In two cases the tests were carried out as early as the 8th day; in both of these the complement-fixation test was still completely negative, whereas the slide-agglutination tests were positive at a titre of 1–80 in each case. Later reactions (16th and 23rd days respectively) were strongly positive with both tests.

In the discussion of the results the author states that the reliability of the test in the differential diagnosis of classic and murine typhus is open to the same criticism as applies to the complement-fixation test.

He also points out that the sera of rabbits and guineapigs infected with murine rickettsiae show cross agglutination with classic rickettsiae to a higher

degree than is the case when the animals are infected with classic rickettsiae and the sera are tested against murine rickettsiae ; he suggests that there are probably more classic elements in the murine antigen than murine elements in the classic antigen. He regards this finding as being in keeping with the evidence produced by himself that murine vaccines give greater cross protection than classic vaccines. *John W. D. Megaw.*

Silva-Goytia, R. Fijación de complemento con sueros de enfermos de tifo exantemático. [**Complement Fixation in Sera of Typhus Patients.**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1944, Dec., v. 5, No. 4, 241–5. English summary (8 lines).

The author employed the technique described by Plotz except that the antigen used was a preparation of animal-lung rickettsiae. The results are not given in detail, but they are stated to have been generally comparable with those obtained by Plotz, who examined specimens of the same sera.

Using murine and classic antigens, the author tested sera from 300 cases of typhus ; most of the subjects had been attacked in Mexico City between 1936 and 1944. Of the sera, 239 reacted more strongly with the classic antigen, and 31 with the murine ; in the remaining 30 the titres were much the same with both antigens. These results are regarded as confirming the opinion of Castañeda and Silva that the typhus of Mexico is predominantly classic in type [see this *Bulletin*, 1940, v. 37, 259]. *John W. D. Megaw.*

Golden, A. **Morbid Anatomy of Typhus as seen in a recent Guatemalan Epidemic : Observations on the Disease.** *Arch. Pathology.* 1945, Apr., v. 39, No. 4, 226–31, 7 figs.

The abundant material investigated by the author was obtained from the bodies of ten persons who had died of epidemic typhus in a mental diseases hospital in Guatemala. The paper is illustrated by ten good photomicrographs.

Interstitial myocarditis, ranging from slight to severe, and patchy in its distribution, was seen in every case. The muscle fibres of the affected patches were separated from each other by oedema and infiltrations of mononuclear cells with a few polymorphonuclears. Occasionally, necrosis of the muscle fibres was seen. No close relationship could be observed between the patches of myocarditis and vascular lesions.

Throughout the central nervous system the lesions were intimately related to small arteries and arterioles affected by endothelial hyperplasia and proliferation, and often surrounded by one or more layers of glial cells. Vacuolation of the nervous tissue was common, so also were perivascular haemorrhages and zones of necrosis. Fränkel's nodules were found in large numbers ; these contained varying numbers of glia cells and their relationship to the affected blood vessels was frequently obvious. In the leptomeninges there were patches of round-cell meningitis. The pia-arachnoid meshes were oedematous and were infiltrated by lymphocytes, plasma cells, and large mononuclear phagocytes.

Some of the gland cells of the adrenals were necrosed. In the spleen, haemorrhagic] foci or zones of necrosis, sometimes both of these, were seen. Hypoplasia of the liver cells was not uncommon ; occasionally also there were zones of necrosis in the liver. The exanthematic plaques in the skin showed vascular lesions similar to those seen in the central nervous system. Some of the renal tubules contained yellow or brown homogeneous casts of haemic origin,

and sometimes red-blood casts were seen. Occasionally also there was subacute interstitial nephritis, but no vascular lesions were found. In the testes the characteristic vasculitis was conspicuous ; it was often accompanied by thrombosis and perivascular round-cell infiltration.

The author regards the condition of haemoglobinuric nephrosis as being similar to that occurring in cases of extensive burns or of the " crush syndrome."

The absence of any obvious association between the lesions and vascular changes was a striking feature of sections of the myocardium, meninges, adrenals, kidneys, liver, and spleen.

The author states that one can only speculate on the after-effects that would result from the necrotic lesions of the central nervous system when they occur in patients who survive ; the healing of such lesions could only be by neural scar formation. *John W. D. Megaw.*

Roth, V. E. **Reactions to Typhus Vaccine.** *Bull. U.S. Army Med. Dept.* 1945, May, No. 88, 111–13.

In a footnote to this article the editor of the journal in which it appears states that millions of doses of egg-yolk vaccine have been given and that the number of reactions has been negligible ; desensitization is not recommended.

Of the 32 reactions seen by the author 23 were of the usual type, with moderate fever, chills, and malaise ; the remaining 9 were allergic, with gastrointestinal, urticarial, or asthmatic symptoms, or with combinations of these. The onset was explosive with eosinophilia ; there was no fever.

Cox, who was consulted, regarded the allergic reactions as due to residual egg antigen contained in the vaccine and stated that the quantity of this residue had recently been greatly reduced.

Four of the patients were definitely allergic to eggs ; three others gave a history of different forms of allergy. *John W. D. Megaw.*

Stowman, K. **Typhus during the War.** *Epidemiological Information Bull.* (UNRRA Health Division). Washington, D.C. 1945, Apr. 30, v. 1, No. 7, 289–310.

Blanc, G. & Baltazard, M. Revue chronologique des recherches expérimentales sur la transmission et la conservation naturelles des typhus. [**Chronological Review of Experimental Research on the Transmission of Typhus and the National Conservation of the Rickettsiae.**] *Arch. Inst. Pasteur du Maroc.* 1944, Oct., v. 2, No. 4, 535–77.

Liu, W. T. **Studies on the Murine Origin of Typhus Epidemics in North China. 3. Isolation of Murine Typhus Rickettsia from Rats, Rat-Fleas and Body-Lice of Patients during an Epidemic in a Poor House.** *Chinese Med. J.* Washington, D.C. 1944, Apr.–June, v. 62, No. 2, 119–39. [32 refs.]

The author regards the present investigation as " completing the evidence of the murine origin of epidemics of typhus fever " in Peiping, where he had already investigated the problem and had found reason to believe that murine rickettsiae could be transmitted from man to man by lice. [See this *Bulletin*, 1942, v. 39, 143 and 144.]

In a poorhouse, with 350 inmates living in overcrowded and insanitary conditions, the disease was detected in February 1941 ; the numbers of cases in that and the following months were : 6, 3, 19, 11, 2 and 4. There were 6 deaths, 4 of which were in children ; presumably many of the adults had been immunized by previous attacks.

Murine strains of rickettsiae were isolated from :—two rats ; two lots of rat fleas (one was *Ceratophyllus anisus*, the other *Xenopsylla cheopis*) ; three

lots of rat mites (*Liponyssus bacoti*); and three lots of human lice from the clothing of patients. No evidence of infection could be found in human fleas (*Pulex irritans*) or in bedbugs; there was doubtful evidence of infection in unidentified ticks collected from some of the rats. No lice were found on any of the rats that were examined.

[The author's findings do not seem to provide final evidence that the attacks were louse-borne. The outbreak occurred during the season of greatest prevalence of rat fleas; this is stated to have been February to September.]

John W. D. Megaw.

MOREHEAD, J. F. **Scrub Typhus from an Epidemiological Viewpoint.** *Bull. U.S. Army Med. Dept.* 1945, May, No. 88, 95–7.

This note deals with the epidemiological conditions observed during an outbreak of scrub typhus among the staff of a large hospital which had just been established on a South-Pacific island. The buildings occupied an area of one-half mile square on a plain between mountain and sea and surrounded by jungle. The area was covered by *kunai* grass six feet high.

There were 71 cases; the highest incidence was among the mess personnel, who were most exposed to contact with rats. Infection in several instances was traced to small, sharply defined areas; several cases occurred in a unit encamped on a site less than 100 yards in diameter.

The incidence dropped sharply after the adoption of the following measures of control—(1) trapping rats (2) cutting and burning of *kunai* grass by native labour; (3) spreading sand over the hospital area; (4) wearing leggings; (5) the liberal use of the repellents, dimethyl phthalate and "612."

The infection was exceptionally virulent and a large proportion of the staff was attacked.

John W. D. Megaw.

WALSH, N. **An Epidemic of Tick Typhus in East Africa.** *East African Med. J.* 1945, Jan., v. 22, No. 1, 11–14.

During the period May–August 1944, 30 Italian prisoners of war were attacked by tick typhus in "East Africa." None of the patients became seriously ill.

In every case there was a history of one or more bites by ticks which infested the tall grass of the camp site and the numerous dogs in the camp. A painless local lesion was found in every case, but this was never at a site from which the patient had removed a tick. The lesion is described as "lenticular, about three-quarters by half an inch," it is surrounded by a narrow zone of inflammation and congestion. The centre became pale after a few days and developed into a small papule which later became a central eschar. The discrete morbilliform rash was most abundant on the chest and abdomen; the legs were much less affected, the face and scalp were invaded in five cases, the soles in one, but the palms were not affected.

Early tenderness and enlargement of the inguinal glands occurred in all the cases; some other gland group, most often the cervical, was affected later.

The onset was rapid; the temperature fell to normal with the appearance of the rash, about the 5th day, gradually rose again and remained high for 4–7 days; the fall was by lysis.

The chief symptoms were, frontal headache, insomnia, depression, and anxiety. Leucopenia was usual; in three patients there was mild leucocytosis.

In 23 cases the Weil-Felix reaction was negative. All the seven positive sera agglutinated *Proteus OXK* at titres of 1–25 or 1–50; two also agglutinated *Pr. OX19* (1–25 and 1–50), and one agglutinated *Pr. OX2* at a titre of 1–25.

John W. D. Megaw.

Tovar, R. M. Rickettsioses exantematicas transmitidas por garrapata en America. [**Exanthematic Rickettsioses transmitted by Ticks in America. (Tick-Borne Typhus Fevers.)**] *Medicina.* Mexico. 1945, Mar. 10 & 25, v. 25, Nos. 479 and 480, 65–85 ; 89–96, 9 figs. [71 refs.]

In this thesis the author gives a succinct and fully-documented account of all the most important work that has been done in the American Continent on tick-borne typhus fever. The bibliography contains 71 references. Some of the author's conclusions are of interest. He states that yolk-sac cultures cannot be obtained in sufficient strength and purity for their successful use in the preparation of vaccines against tick-borne typhus or in carrying out the complement-fixation test. He favours the use of a vaccine prepared from infected ticks.

He states that tick-borne typhus is regarded as the most widely distributed rickettsial infection in America, and that it probably occurs in many places where it has not yet been detected. The virulence of the infection is exceedingly variable ; diagnosis is often very difficult, and may be impossible without a complete laboratory investigation.

The disease may often be missed because a positive Weil-Felix reaction is commonly regarded as being diagnostic of endemic typhus and the possible occurrence of the tick-borne disease is not taken into consideration.

Tick-borne typhus closely simulates flea-borne typhus in its clinical, pathological, and immunological characters, so that a unitary aetiology of these two diseases is suggested. *John W. D. Megaw.*

Mariotte, C. O., Bustamante, M. E. & Varela, G. Hallazgo del *Ripicephalus sanguineus* latreille infectado naturalmente con fiebre Manchada de las Montañas Rocosas en Sonora (Mexico). [**Specimens of** *Rhipicephalus sanguineus* **found naturally infected with Rocky Mountain Spotted Fever in Sonora (Mexico).**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1944, Dec., v. 5, No. 4, 297–300, 1 graph. [11 refs.] English summary (2 lines).

Rickettsiae isolated from a batch of *Rhipicephalus sanguineus* from a dog in Chinal caused scrotal reaction and death in guineapigs.

Guineapigs recovered from " exanthematic typhus " were susceptible to the strain, but other guineapigs that had survived infection by Rocky Mountain spotted fever were immune. *John W. D. Megaw.*

YELLOW FEVER.

Colonial Office. **Fourth Interim Report (being a Revised Version, with certain Additions and Appendices, of the Third Interim Report) of the Inter-Departmental Committee on Yellow Fever Control.** 1944, December, 18 pp. [Miscellaneous No. 503B.]

[Permission to publish this review has been obtained from the Controller of His Majesty's Stationery Office.]

The dislocation of the activities of the Office International d'Hygiène Publique in Paris in the summer of 1940, together with the extension of the theatres of war and the rapid opening of the new routes of communication, called for the formation of some body to suggest further means of control of yellow fever in Africa. This matter was brought to a head by the severe outbreak of yellow fever, which occurred in the Anglo-Egyptian Sudan in 1940–41. As a result of co-operation between the Colonial Office and the War Department in London, an Inter-Departmental Committee was set up consisting of representatives of

the Armed Forces, the Government Departments, and the regions of the Commonwealth which were concerned. Individuals who have been actively engaged in Yellow Fever research in England and America were consulted at various times on particular aspects of the problems as they arose.

A number of recommendations have been made concerning the most important measures of control that should be encouraged.

Strict control of *Aëdes aegypti* and other potential mosquito vectors of yellow fever should be carried out, particularly in the vicinity of aerodromes, warships and ports, and at stopping places along transport routes.

Anti-*Aëdes* services should be maintained permanently, with adequately trained staff, in order to keep the *Aëdes Index* at not more than 1 per cent. at any time of the year.

The necessity for early detection and correct diagnosis of the disease, followed by notification and isolation of cases should be stressed to all medical and other personnel likely to be concerned. Because of the difficulty of clinical differentiation between mild cases of yellow fever and other febrile conditions, it is recommended that in endemic areas samples of blood should be collected for yellow fever immunity tests from all cases of fever in which no obvious cause is detected. Blood should be collected in the acute stage, and again three weeks later in all suspected cases in which recovery takes place. If, on the other hand, the patient dies within ten days from the onset of the illness, a specimen of liver tissue should be taken and sent to the nearest laboratory that undertakes the histological diagnosis of yellow fever. It is recommended that viscerotomy services be maintained in endemic areas as the surest method of detecting yellow fever.

All travellers by land, sea and air, within or passing through the endemic areas, as well as all non-Africans living in the areas, should be inoculated against yellow fever with a potent vaccine. Supplies of vaccine are maintained in England, U.S.A., South America, and West and East Africa. Persons inoculated with a normal immunizing dose of a potent vaccine are protected on and after the tenth day, calculated from the day of inoculation. [The scientific evidence on which this statement is based is included in an Appendix to the report.] Inoculation is accepted as providing protection for four years. An attack of yellow fever confers lifelong immunity, and persons who have recovered from the disease need not be inoculated or subjected to quarantine. The committee also recommend that guards and regular staff of aerodromes should be immunized and that casual labour employed on aerodromes should be immunized to the fullest extent possible.

Any individual who is travelling from yellow fever endemic areas to those where yellow fever does not exist, but in which there may be conditions which permit of its development, and who does not carry a valid inoculation certificate, should, at the first recognized stopping place in the latter areas, be quarantined in properly screened quarters until *six days* have elapsed from the date of leaving the endemic area. Any suspected individual who shows a rise of temperature on or before the sixth day should be kept in quarantine until the cause is determined.

[" *A valid inoculation certificate is one certifying—*

" (i) That the bearer has been inoculated for the first time more than ten days and less than four years previously ; or

" (ii) That he has been re-inoculated within the past four years ; or

" (iii) That he has recovered from an attack of yellow fever and that his blood contains immune bodies against yellow fever as proved by a test carried out by an Institute regularly carrying out biological tests for yellow fever."]

The Committee consider that insufficient attention has been directed to the effective disinsectization of all aircraft moving within or through endemic areas. The insecticide should be applied by hand-spray connected to a supply of air under pressure, or by apparatus of the Aerosol bomb type. Disinsectization should be carried out on departure of the aircraft from the last airport in an endemic area and on its arrival at the first airport of call in a non-endemic area.

A building-free zone of 440 yards should be maintained around the perimeter of all aerodromes. Guards may be housed within the boundaries provided they are immunized, but casual labour should not live within the area. The term *Anti-amaryl* should no longer be applied to any aerodrome; all aerodromes must be considered potentially infected if they are in an endemic area.

F. O. MacCallum.

Afrique Occidentale Française: Rapport sur le Fonctionnement Technique de l'Institut Pasteur en 1943 [Durieux, C.]. 59–70. Service de la fièvre jaune. [**Yellow Fever Service.**]

The yellow fever virus used for vaccination was a French strain which was isolated at Dakar in 1927 and had sustained 257 passages; no further animal passages were made during 1943 as it was thought better to keep the dried virulent mouse brain in the refrigerator and so safeguard the success of the inoculations needed for the preparation of the vaccine. During the year, 4,097,000 doses of dried vaccine were made and 41,960 ampoules of 2 cc. of gum arabic solution for the suspension of the vaccine, at the time of use. Altogether, 2,958,349 persons were vaccinated, 10,275 being of white race. The vaccine was used either alone or mixed with smallpox vaccine, and vaccination was done by scarification of the skin. By the end of the year 1943, at least half the population of French West Africa had been vaccinated.

In 1943, as in preceding years, it has been very difficult, owing to shortage of suitable food, to maintain a supply of white mice for protection tests, and this has frequently hindered the work. The need for an animal breeding station was urgent and 37 hectares [about 90 acres] of land were acquired about 16 miles from Dakar; it was hoped to begin the construction of four animal houses, stores and a house for the European manager, early in 1944.

Protection tests.—During 1943, the blood serum of 67 persons was tested, 45 to test the effectiveness of vaccination, and 22 for the diagnosis of yellow fever; of the former, 44 had received the vaccine of the Dakar Institute, five subcutaneously and 39 by scarification, using Laigret's egg-yolk method. The five former persons had been vaccinated six years, eight years (2) and nine years (2) before the test; all the sera were strongly positive. In a table showing all the tests made by this method it is seen that 95 per cent. of 713 sera were positive [441 were tested less than one year after vaccination and 107 at 1–2 years] and 85·9 per cent. were strongly positive; of 29 vaccinated 5–9 years before, 26 had positive and 25 strongly positive sera.

The results of scarification were equally good; 37 of the 39 [36 tests within two years after vaccination] being positive and 35 strongly positive. A table shows that of a total of 2,403 persons vaccinated by scarification [2,390 tested within two years after vaccination] 95·8 per cent. were positive and 83·8 per cent. strongly positive. [The number of mice used in the tests is not given.]

Diagnostic tests.—Nineteen of the 22 sera were taken during the course of an illness or immediately afterwards; six gave a strongly positive result, thus excluding a diagnosis of yellow fever, one was weakly positive and was probably a case of a late reaction to vaccination, and the other 12 were negative. Two of these 12 persons, however, had strongly positive sera after recovery, thus confirming the diagnosis of yellow fever, and in three fatal cases the diagnosis of

yellow fever was confirmed, after death in two, and by isolation of the virus in the third. The other seven (natives) remained doubtful as they became unavailable for testing.

Samples of blood from 14 sick persons were inoculated into white mice; four of the patients were found to have yellow fever, by post-mortem examination or by serum tests, but virus was isolated from one only. Examination of the livers of 32 people showed that 10 had died of yellow fever.

Yellow fever in French West Africa.—Twelve cases of yellow fever (eight in Europeans and four in Africans) were diagnosed during the year, 10 being fatal; three were in Senegal, eight in Guinea, and one in the Ivory Coast. As in the preceding years, most of the cases seemed to be related to a reservoir in wild animals, since infections occurred in persons living isolated in the "bush" or in very sparsely populated places. Only one of the patients, a European, had been vaccinated against yellow fever, and his serum had never been tested, but the vaccine used had been proved to be active by tests on others who were vaccinated at the same time and place. It is thought that this patient either could not develop antibodies or that they had disappeared very quickly. The author states that some persons, if not watched, will remove the vaccine before it has had time to enter the skin. *J. F. Corson.*

PLAGUE.

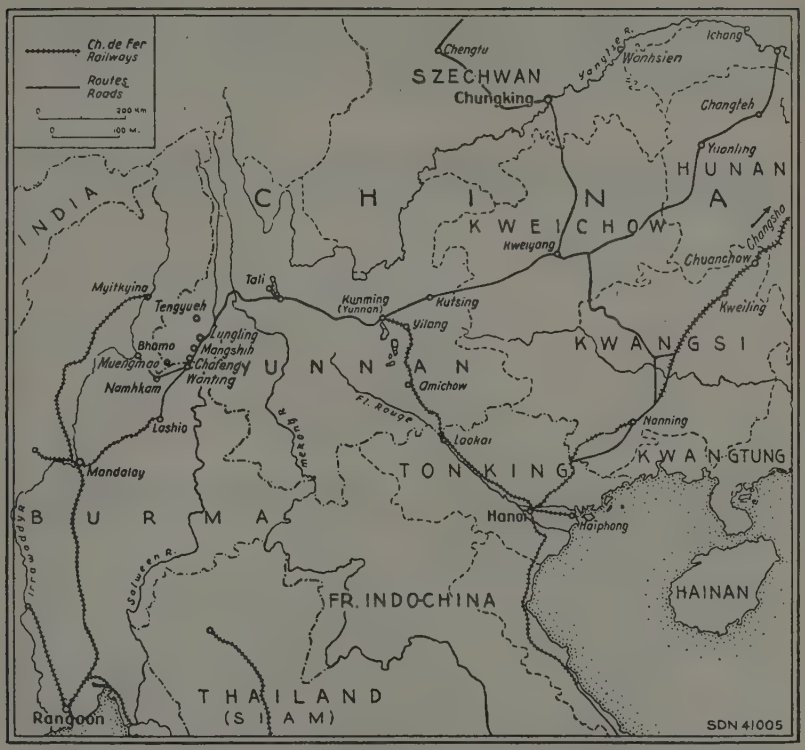
Epidemiological Information Bull. (UNRRA Health Division). Washington, D.C. 1945, Feb. 28, v. 1, No. 4, 169–70. **Plague Outbreak in Western Yunnan, China.**

Plague has been endemic near the border between northern Burma (Shan States) and the Yunnan Province of China for a long time, and breaks out almost every year in neighbouring villages. In 1939 a severe outbreak occurred at Nankham as a result of movements of population and the employment of labour for the opening of the Burma Road, which ended then at Teng-Yueh (Tengchung). Early in 1940 bubonic plague occurred in Yunnan Province at Mungmao near Shweli River, and later at Cheshinkai and Nwangtao; on the Burma side of the border it appeared at Muse (opposite Mungmao), Selang and Namkham in the Bhamo district.

In January 1945, the National Health Administration of China stated that bubonic plague had broken out around Tengchung (Teng-Yueh) situated a few miles west of the Burma Road, and also at Nangtien, 25 miles south of Tengchung. A medical expedition to the area was organized and a preliminary report has been received from Dr. Y. N. Yang, Senior Technical Expert of the National Health Administration.

Plague appeared in September 1943 at Talungchuan, about two days' walk from the Burma border; in this village of 1,000 families, 140 deaths occurred from February to May 1944. In June 1944, plague occurred in a group of about 50 villages, called Lo Pu Shih Chuan, about two days' walk north of Talungchuan; there were 136 cases and 105 deaths, chiefly in July and August. Some cases also occurred at Chi Mu Tsai, north of Lo Pu Shih Chuan.

The outbreak at Tengchung (Teng-Yueh) was reported early in October 1944, and at Nantien early in November; up to January 9, 1945, there were 102 cases and 23 deaths. The incidence was highest among children and young adults, but the case mortality was 11·4 per cent. in the group under 30 years of



Map of the Yunnan Province of China in relation to bordering countries and the Burma Road.

[Reproduced from the *Bulletin of the Health Organisation, League of Nations.*]

age and 50 per cent. in those over 40 years. Sixty-nine of the 102 patients had had one to four inoculations of plague vaccine ; the mortality rates were 14·5 per cent. in inoculated, and 41·4 per cent. in uninoculated persons.

Sulphathiazole, sulphadiazine and serum were used in treatment ; sulphadiazine gave the best results—one death in 27 cases—but the author reserves a final opinion on methods of treatment.

Many dead rats were found in the villages where human plague occurred.

J. F. Corson.

Shih, F. I. & Pollitzer, R. **Some Observations on the relation between Rodent and Human Plague.** *Chinese Med. J.* (Chengtu Edition). 1944, Jan., v. 62A, No. 2, 45–51, 4 graphs.

The rodents referred to in this article are not sylvatic but domestic, the chief cause of human plague. An account is given, more or less in diary form, of the correlation between degree of incidence of plague in the rat population and its seriousness for the human population. It is illustrated by graphs and tables, and the argument used is that a forecast can be made, " at least under the conditions obtaining in Central China," of the imminence of a critical situation, by close study of the frequency with which plague is occurring among rodents.

A conclusion is worded thus :—" . . . the situation remains reassuring as long as the incidence of infected rodents remains well below 20 per cent. The condition must be considered as critical when this level is approached or reached . . . human plague becomes imminent if a level of 25 per cent. is reached or exceeded."

W. F. Harvey.

POLLITZER, R. & LI, C. C. **Some Observations on the Decline of Pneumonic Plague Epidemics.** *Chinese Med. J.* (Chengtu Edition). 1944, Jan., v. 62A, No. 2, 52–5.

China must have vivid recollections still, if only in the literature of the subject, of pneumonic plague. Reference is made by the authors to the usual statements that decline of pneumonic plague in a community is due to the measures adopted or to seasonal influence. Their own analysis of their cases, recorded in detail, leads to the conclusion that the occurrence of primary pneumonia in plague depends on contact with a patient already suffering from pneumonia and exhibiting a bloody sputum and cough. When patients begin to show absence of these features the plague becomes non-pneumonic and the epidemic is declining.

W. F. Harvey.

SHIH, F. I., CHANG, S. S. & YUAN, K. L. **A Report on some Simple Measures for the Control of a Rural Plague Outbreak.** *Chinese Med. J.* (Chengtu Edition). 1944, Jan., v. 62A, No. 2, 56–60.

The measures described have reference to two towns of about 1,800 and 1,700 inhabitants. Many of these were of the usual antiplague description, such as quarantine, anti-rat and anti-flea measures and rat poisoning. In one of the two towns plague seemed to be restricted to the northernmost part, which could be segregated, and was segregated, by cutting a connecting bridge over a strip of water and by digging a 10-foot ditch to cut off communications. Pickets of soldiers were employed to enforce segregation and watch was kept to prevent inhabitants from taking patients or dead bodies out of the plague area, carrying out bedding and household goods and making journeys which had no relation to business. " All cotton shops in the segregated area were closed and their stocks sealed. Export of rice, cotton and other goods apt to harbour fleas . . . was prohibited." Material destined for the army, consisting of 2,000 bales of cloth, had to be allowed export and was disinfested mechanically by exposure to air and sun. The description is useful in showing how special measures may have to be adopted, applicable mainly to local conditions.

W. F. Harvey.

HSUE, L. T. **Experimental Studies on Living Plague Vaccines.** *Chinese Med. J.* Washington, D.C. 1944, Apr.–June, v. 62, No. 2, 193–6.

Comparisons have been made of the protection afforded in guineapigs by dead plague vaccines and by agar slope cultures of attenuated living organisms. Attenuation was effected by growing virulent plague bacilli, obtained from the inguinal gland of a fatal case of plague, at 41–42°C. The strain was well attenuated after 16 months of subculture and by the 733rd generation. A testing subcutaneous injection of virulent bacteria obtained from the spleens of rats infected with virulent culture was given three weeks after immunization with various doses of attenuated organisms, and immunization was considered to be satisfactory if the guineapigs were still alive one month later. A secondary research was made into the power of living plague vaccines to penetrate to the internal organs. Results are summarized as follows :— (1) All dead antiplague vaccines used were unsatisfactory. (2) Attenuation of virulent plague bacilli

could be effected by subculture at high temperature. (3) A spontaneously attenuated strain, "Ming 2," had much better immunizing power than the artificially attenuated organism. (4) The antigenic potency of living plague vaccines is higher the further they can be shown to diffuse from the site of injection to internal organs. *W. F. Harvey.*

Devignat, R. L'aération des milieux liquides de culture par barbotage d'air. Le bacille de Yersin en milieu aéré. Observations complémentaires. [**Aeration of Fluid Culture Media. *P. pestis* in Aerated Media. Supplementary Observations.**] *Rec. Travaux Sci. Méd. Congo Belge.* 1945, Jan., No. 3, 112–19. [18 refs.]

This is a version in French of the paper abstracted in this *Bulletin*, 1944, v. 41, 668.

CHOLERA.

Burrows, W. **The Endotoxin of the Cholera Vibrio : Isolation and Properties.** *Proc. Soc. Exper. Biol. & Med.* 1944, Dec., v. 57, No. 3, 306–8. [10 refs.]

Both the Inaba and Ogawa vibrio types were used and toxic solutions of the cell substance have been prepared in the following ways :—(*a*) Disintegration by high speed grinding for 4–5 hours with sand to obtain a toxic opalescent supernatant fluid ; (*b*) solution of cells in 6 M urea ; (*c*) digestion with pepsin 3–5 days without inactivation of the toxicity, and centrifugation to give a toxic supernatant fluid ; (*d*) extraction in the cold with M/2 trichloracetic acid, which was the first method used ; (*e*) extraction of lyophilized cells with methyl alcohol, ethyl alcohol, chloroform or ethyl ether. The extracted material appeared to be a mixture of lipids, contained inorganic salts, was yellowish in colour and was negative to the Molisch, Millon and biuret tests in alcoholic solution or in aqueous suspension. It could be consistently obtained with a mouse m.l.d. of 30μg. In general it became clear that : "the endotoxin of the cholera vibrio is (*a*) resistant to peptic or tryptic digestion, (*b*) stable to acid, (*c*) unstable to alkali (N/10 NaOH at room temperature), (*d*) readily soluble in methyl and ethyl alcohols, chloroform and ether but not in glycols, (*e*) readily dialyzable, and (*f*) is closely associated, possibly identical, with a phospholipid." *W. F. Harvey.*

Burrows, W., Mather, Adaline N., Wagner, Sylvia M., & McGann, Virginia G. **The Endotoxin of the Cholera Vibrio : Immunological Properties.** *Proc. Soc. Exper. Biol. & Med.* 1944, Dec., v. 57, No. 3, 308–11.

Some of the work which has previously been done is irrelevant because it relates to a toxic haemolytic vibrio, whereas the true cholera vibrio is non-haemolytic. Various preparations of cholera endotoxin have been studied by the authors and immunological activity demonstrated by skin reactions in immune rabbits, by specific precipitation and by complement fixation with rabbit immune sera. These tests appear to show that endotoxin preparations have haptene-like functions although the antigen-antibody reactions have not proved useful for routine purposes. It has been found possible to immunize mice actively by inoculation of alcohol-saline suspension of alcoholic endotoxin. "On the other hand it has not been possible to demonstrate *in vitro* neutralization of the activity of endotoxin preparations by either antibacterial or anti-endotoxic sera known to be protective when tested against mucin-vibrios in the mouse." *W. F. Harvey.*

BURROWS, W., WAGNER, Sylvia M. & MATHER, Adaline N. **The Endotoxin of the Cholera Vibrio : Action on Living Semipermeable Membranes.** *Proc. Soc. Exper. Biol. & Med.* 1944, Dec., v. 57, No. 3, 311–14, 1 fig.

As the diarrhoea of cholera is attributed to toxic action it might be expected that the living membranes of immunized animals would show alteration in permeability to fluids. One of the tests made was to use pieces of intestine from freshly killed rabbits, stretched over glass tubing, 5 mm. in diameter, under 8 to 10 inches of hydrostatic pressure and observe the rate of flow of Ringer-Locke solution across this semi-permeable membrane. The experiments which are set out in graph form, were :—with normal control rabbit, normal rabbit plus toxin, immune control, immune rabbit plus toxin with resulting flow of 0·25 cc., 0.55 cc., 0.27 cc. and 0.30 cc. per hour respectively. Acceleration of flow began to be apparent at a concentration of toxin of 0·5 m.l.d. (mouse) per ml. and increased steadily to double its rate at 4 m.l.d. without any apparent deleterious effect on the intestinal membrane. If the increased permeability was produced by suspensions of living vibrios the addition of antiserum agglutinated the bacteria and annulled the increase of permeability, but this effect was not produced when the antiserum was added to the endotoxin. Strips of intestine from immune animals were quite unaffected in permeability by addition of toxin and behaved like normal control rabbit intestine. " It is apparent that active immunity to Asiatic cholera in the experimental animal, and presumably also in man, includes antitoxic as well as antibacterial immunity," and " if it be assumed that the resistance of the immune intestine to the action of the endotoxin has an antigen-antibody basis . . . it is clear that the functional antibody cannot be circulating . . . in the isolated intestine and may, therefore, be intracellular . . ., presumably in the macrophages of the tissues of the intestine." *W. F. Harvey.*

BACILLARY DYSENTERY.

SCOTT, R. B. **On the Effect of Sulphaguanidine in Acute Bacillary Dysentery.** *J. Roy. Army Med. Corps.* 1945, Apr., v. 84, No. 4, 159–62, 1 fig. [13 refs.]

" In the hope of providing some indication of its [sulphaguanidine] value a comparative analysis has been made of the recovery rate of patients admitted to a military hospital in the Middle East with bacillary dysentery in 1940 and 1943.". The number of days in hospital was taken as an index of the recovery rate. The author gives reasons for regarding the two series of cases as comparable as regards the nature and severity of the infections and the conditions under which they were treated.

The treatment given in 1940 was saline purgation with restriction of diet ; in 1943, patients with bacillary dysentery were treated with sulphaguanidine.

Figures of the number of admissions, the incidence of types of bacteria isolated, and the length of stay in hospital are shown in tables. The mean length of stay in hospital was 12·7 days in 1940 and 11·6 in 1943 ; this difference is statistically significant. It is uncertain how much this decrease was due to the use of sulphaguanidine and how much to the discontinuance of purgation. It is emphasized that the observations are applicable only to the mild type of bacillary dysentery prevalent in the Middle East [see, however, the views of BOYD and of SCADDING, this *Bulletin*, 1944, v. 41, 755]. *J. F. Corson.*

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS.

Browne, D. C., McHardy, G. & Spellberg, M.A. **Statistical Evaluation of Amebiasis.** *Gastroenterology.* 1945, Feb., v. 4, No. 2, 154–62. [10 refs.]

A statistical study of amoebiasis is liable to be influenced by a variety of factors. The carrier incidence of this communicable disease in civilians is estimated (in U.S.A.) as from 10 to 20 per cent. Moreover these carriers have an estimated " asymptomatic phase " varying from three months to thirty years.

The term amoebiasis includes a number of widely different clinical states and it is recognized that fairly extensive lesions of the intestinal tract may coexist without producing any positive external evidence of their presence. There is a predominant frequency of the disease in males of the third and fourth decades—a fact which emphasizes its important relationship to the military forces and defence workers.

Prognosis in amoebiasis really includes an assessment of future morbidity as well as of mortality. The proper application of this term should be " forecasting the outlook " of the disease.

The present survey covers 3,984 consecutive ambulatory gastrointestinal patients, 4,299 admissions to the gastrointestinal services at Touro Infirmary from 1936–1943, with the addition of 740 admissions to La-Garde General Hospital from January, 1942 to July, 1943.

All the 790 amoebiasis patients were residents of Louisiana or neighbouring states. There were 429 males and 361 females with an average age of 38·3 years. In private practice the incidence of amoebiasis encountered was 14·1 per cent. of gastrointestinal patients seen, contrasted with 5·2 per cent. in hospital cases.

Radiographic examination claims a place in amoebiasis, in demonstration of diaphragmatic alteration with hepatic complications. Barium enema studies are of minimal value, though 35·5 per cent. in this series showed changes consistent with amoebiasis. In two instances, the granulomata were demonstrated and responded to specific therapy, whilst a third, involving the transverse colon, was subjected to operation.

Diagnoses of amoebiasis were made in 42·2 per cent. of proctoscopies on " active amoebic dysenteric patients." Although fever is rare in amoebiasis, and is generally considered " to form part of the picture only in the complications," nevertheless it was found in 7·4 per cent. of the uncomplicated cases.

In therapeutic evaluation the following drugs were employed :—emetine, carbarsone, anayodin, diodoquin, vioform, and sulphamido derivatives. In a great many instances, the drugs were combined and frequent repeated courses of the same drug employed. Emetine was not used alone in any instance. The assessment of results which is given in a table in the paper, is based on a three-month post-therapeutic asymptomatic period with three negative stool examinations.

Recurrences, which numbered 50, did not lead to any conclusions other than the statement that no one drug is always a successful and complete amoebicide.

The fatalities numbered 3, or 0·3 per cent. They were due respectively to hepatic and prostatic abscesses, haemorrhage from ulceration and bronchopneumonia. Refractory cases numbered 3. All other recurrences responded to repeated treatment with amoebicides. Thirty-seven " amebic complications " included 6 instances of appendicitis, 1 of prostatic abscess, 15 of hepatitis, 5 of hepatic abscess, 1 of perforation, 6 of granulomata, 2 of subphrenic abscess and 1 of pleural effusion. Concomitant enteric diseases were present in 12·3 per

cent. of the amoebic cases in this series, emphasizing the need for differential diagnosis in evaluating the actual cause of the enteric symptoms; these concomitant conditions were :—

	Cases
Malignancy of colon	6
Benign polyposis	2
Nonspecific proctitis	11
Chronic idiopathic ulcerative colitis	4
Gonorrhoeal proctitis	2
Staphylococcal ulcerative colitis	1
Diverticulosis of colon	6
Caecal volvulus	1
Endometriosia	2
Fistula in ano	8
Anal constriction	14
Lymphogranuloma venereum [? L. inguinale] ...	1
Bacillary dysentery	8
Other enteric parasites	28
Ileocaecal tuberculosis	1

P. Manson-Bahr.

HENNESSEY, R. S. F. **Reflections on Amoebiasis.** *Acta Med. Orientalia* (*Palestine and Near East Med. J.*) 1945, Apr., v. 4, No. 4, 103–8.

In these "reflections" the author lays emphasis on the variability of amoebiasis in regard to the amoeba itself, the host, and the locality where the disease occurs. He points out that with modern methods evidence of infection can be obtained in a large proportion of cases, but a critical attitude should be adopted towards treatment, each case being considered on its merits. Some of the views expressed may be indicated in extracts from the summary :

"There is evidence that *Entamoeba histolytica* and its host reach a stable equilibrium in the great majority of cases, progressive tissue invasion being much less common than is generally considered to be the rule."

". . . antiamoebic treatment should be reserved for patients showing definite signs of tissue damage."

"The invasiveness of *E. histolytica*, and its manifestations in the human body, vary with the race of the host and the strain of the amoeba present. The variations in incidence of hepatitis and liver abscess are notable, and are unlikely to be accounted for by a nutritional factor." *J. F. Corson.*

MCCONAGHEY, R. M. S. **Amoebiasis of the Anus and Perineum, with Report of a Case.** *Indian Med. Gaz.* 1945, Feb., v. 80, No. 2, 79–81. [10 refs.]

The first reference to amoebiasis of the perineum is that of J. L. MAXWELL [this *Bulletin*, 1912, v. 1, 456] who described it as "Fistulous Disease of the Buttocks" and as occurring in South Formosa and also in S. China. Further, it has been known for some time that amoebae can cause ulceration of the skin [*ibid.*, 1939, v. 36, 295], but no instance of amoebiasis cutis of the perineum has been previously reported from British India or Burma, nor, according to the author, has any account of such cases been reported in British Medical literature. [This is certainly not correct, see this *Bulletin*, 1940, v. 37, 121.]

The case reported is one of the Anglo-Burmese woman who suffered from amoebic dysentery in 1942 during evacuation from Burma to India. Subsequently a fungating mass the size of a large walnut, yellow and pink in colour and exuding pus, developed around the anal orifice. From this an ulcer spread forward over the perineum into the posterior wall of the vagina, where the whole area was intensely tender. In the serous exudate, removed from the edge and

floor of the ulcer by capillary tube, abundant motile *E. histolytica* were seen. Definite improvement was noticed 24 hours after the first injection of emetine, and after the fifth the discharge ceased. No signs of dysentery were noted at this time. The patient was discharged on the 18th day free from all symptoms except those referable to the haemorrhoid.

[Frequent references are made to the paper by C. H. Hu (*Festschrift Bernard Nocht*, 1937, p. 221, Hamburg) who described a series of 14 cases in which amoebic infection was present, sometimes as ulceration of already existing papillomata, sometimes as extensive ulceration or even gangrene, usually in the anal region, but also in the urethra, or on the cervix of the female, as well as on the labia majora and minora.] *P. Manson-Bahr.*

Carri, E. L. Entamebiasis intestinal y tuberculosis pulmonar. [*Entamoeba histolytica* **and Pulmonary Tuberculosis.**] *Prensa Méd. Argentina.* 1945, Feb. 16, v. 32, No. 7, 304–10.

The author states in his introductory remarks that in this paper he refers solely to *E. histolytica* and to none of the other entamoebae. [More than half the paper is taken up with general remarks on *E. histolytica* and cyst-passers, giving facts which are well known to readers of this *Bulletin*.] He gives his conclusions based on 36 patients in whom the association of pulmonary tuberculosis and *E. histolytica* existed, but, for want of space, he does not give details of any of them. Of the thirty-six, 27 were men, 9 were women. Twenty-two of them died, but all from the tuberculous disease, none from dysentery; eight recovered; of the other six nothing is known. Four of those who died received treatment for the amoebiasis while none of those who recovered were treated for it. "This means that they relied on their own natural defences, but, seeing the proportion is small, it would not be wise to trust too much to this." Finally, the author admits that he knows of no drug or form of medication which will act upon the entamoeba and its cysts without acting deleteriously also on the general condition. *H. Harold Scott.*

Morton, T. C. St. C. **Diodoquin for Chronic Amoebic Dysentery in Service Personnel Invalided from India.** *Brit. Med. J.* 1945, June 16, 831–3.

The problem of treating resistant amoebic dysentery has aroused great interest, and the author here reports a clinical trial of "Diodoquin" in a series of R.A.F. patients invalided from India. Two of these had received no previous specific therapy, but all the others had had repeated maximum courses of emetine injections (12 gr.), with or without any further gut-sterilizing treatment, such as E.B.I. by mouth combined with quinoxyl retention enemata; all had experienced from 3 to 9 relapses prior to treatment with diodoquin. The majority had also received carbarsone, stovarsol and numerous courses of sulphaguanidine or sulphapyridine.

Diodoquin (5,7-diiodo-8-hydroxyquinoline), produced by the Searle Laboratories of the U.S.A., was first introduced in 1935, and has been favourably reported upon by Craig (1937) and d'Antoni (1942) [see this *Bulletin*, 1941, v. 38, 271 & 1943, v. 40, 697]. It is a tasteless, non-toxic compound, containing 63·9 per cent. iodine (in contrast with quinoxyl which contains 28·97 per cent., and vioform which contains 41·5 per cent.). It is "extremely insoluble" in water, dilute acids or alkalis, and, because of this, it does not produce the unpleasant effects experienced with other hydroquinoline compounds when given by mouth. The makers state that it is not absorbed, but David, Phatak and Zener (1944) report that in some instances it may give rise to *pruritus ani* about the fourth or fifth day of administration, which persists for

some days after the drug is stopped. Increases in the blood-iodine levels from 45·6 microgrammes to 437·25 milligrammes have been noted in man and experimental animals. In the present series of 78 cases, two of intolerance to diodoquin were observed, and two patients complained of mild *pruritus ani*. Diodoquin is opaque to X-rays, and radiographs show an even distribution of the drug throughout the large intestine.

Three tablets of diodoquin (each of 3·2 grains), three times daily for 20 days, was the standard dosage. In addition, in another series of cases, diodoquin was combined with quinoxyl retention enemata for 10 days, and a small series, which showed either amoebic hepatitis or other evidences of deep infections, received emetine injections as well. A small unselected control series, treated with E.B.I. and quinoxyl enemata, has been included for comparison. All the patients were sigmoidoscoped before and after treatment, and in 15 the treatment was carried out on the basis of sigmoidoscopic appearances alone the stools being negative at the time, although in all of them *E. histolytica* had previously been found.

SERIES I. *Twenty-six cases were treated with diodoquin by the mouth.* Seventeen of these were apparently cured; follow-up examinations of three stools were negative two months after discharge from hospital. Two of the patients had received no previous treatment. In addition, in three cases with positive sigmoidoscopic findings, but negative stools, the lesions healed at the end of treatment. There were two relapses, and four cases were resistant. In one of these, amoebic abscess of the liver developed three months later; another patient had an acute relapse, and his case had been particularly resistant to previous forms of treatment. Another presented petechial haemorrhages in the rectum at the end of one course, and yet another relapsed four months after treatment.

SERIES II. *Cases treated with diodoquin for 20 days plus quinoxyl retention enemata for the last 10 days of the course.* This combined treatment was initiated on the grounds that "lesions in the rectum might not be exposed long enough to diodoquin in the lumen of the bowel." Logically, it would have been better to have used diodoquin retention enemata. This was done successfully in one case, but it could not be pursued, as supplies of the drug were restricted. Thirty-nine cases were treated in this series, with results as follows:—22 cured (stools positive for *E. histolytica* before treatment), 8 cured (stools negative, but sigmoidoscopically typical); 2 were resistant, and 7 relapsed.

SERIES III. *Emetine hydrochloride 6–10 gr. by needle plus diodoquin concurrently by mouth for 20 days: for the last 10 days the patient also received quinoxyl retention enemata without a preliminary bowel washout.* This treatment was carried out in those cases showing symptoms of hepatitis, gross deep ulceration or marked leucocytosis. The results were:—9 were apparently cured, having had stools positive for *E. histolytica* before treatment; 2 were apparently cured, having had stools negative before treatment; 1 relapsed; 1 was resistant. In one patient, petechiae were present in the rectum after one course; he was then given E.B.I. and quinoxyl and a further sigmoidoscopy showed a normal mucosa.

SERIES IV. *Standard combined course: E.B.I. 3 gr. in cachets by mouth, together with a cleansing bowel washout of 2½ per cent. sodi bicarb. solution, followed an hour later by 250 cc. of 2½ per cent. quinoxyl, which was retained for 6–8 hours. This treatment was carried out for ten days, and was then followed by carbarsone, 4 gr. b.d. for 10 days.* There were 24 cases in this series; 16 were cured, 6 relapsing. Three primary cases were cured. Two of the relapsed cases were subsequently cured with diodoquin. In 5, examination of the stools was negative, but sigmoidoscopy showed either ulcers or pits. Two cases were resistant to all forms of treatment.

Two instances of intolerance to diodoquin were encountered. One patient, on the 14th day of treatment with this drug, had abdominal pain, diarrhoea, blood and mucus in stools full of *E. histolytica*. He responded well to emetine, and tolerated a second course of diodoquin and quinoxyl retention enemata, with no further ill effects. The second, a severe case, with Dyak-hair sloughs in the rectum and *E. histolytica* in the stools, complained on the 14th day of abdominal pain, diarrhoea and headache. The symptoms were rapidly relieved by emetine. A further course of diodoquin, E.B.I. and quinoxyl was well tolerated, and sigmoidoscopy showed complete healing of the ulcers.

The histories of two specially severe cases are given : one was treated with diodoquin alone, the other received a course of emetine plus diodoquin. The first exemplified how, by erratic and inefficient initial therapy, a case is rendered emetine resistant, and how quickly it may respond to diodoquin. The second had had unrecognized amoebiasis of over 24 years' standing before the correct diagnosis was made. In October 1944, the stools were found to contain active *E. histolytica*, which emanated from a large rectal amoeboma, 4 in. from the anus, suggestive of an adenocarcinoma. On a course of six daily 1 gr. injections of emetine together with diodoquin for 20 days, and treatment with quinoxyl retention enemata and stovarsol this amoeboma healed up. The patient subsequently received a 10-day course of E.B.I. and quinoxyl. Three months later, sigmoidoscopy revealed a normal mucosa.

Diodoquin, then, " appears to be the best of the oxyquinoline group of drugs in the treatment of amoebiasis," and is a valuable addition to the list of remedies. It is non-toxic in therapeutic doses. The practice of treating amoebiasis with emetine alone cannot be too strongly condemned, as only a small percentage of cases are cured, whilst the vast majority are rendered more resistant to further treatment with emetine and less amenable to other available drugs. *P. Manson-Bahr.*

Cheng, Wen-Szu, Liu, You-Ping & Tan, Shih-Chien. **Toxicological Investigation on Ya Tan Tzu.** *Chinese Med. J.* (Chengtu Edition). 1944, July, v. 62A, No. 4, 133–9. [10 refs.]

Ya Tan Tzu, the seed of *Brucea javánica*, has been given in China for the treatment of dysentery during the past 180 years, perhaps longer, but it composition and mode of action have never been closely studied ; at all event no very conclusive results have been reached. Some have reported the active principle to be a glucoside, others a saponin, others again an alkaloid.

The authors have obtained and tested the expressed oil, a volatile oil distilled by steam from this, ether-, chloroform-, and alcohol-extracts of the oil-free portion, using cats, dogs and rabbits as their experimental animals, and administering the various preparations by stomach-tube and by injection, hypodermic and intravenous.

It is the oil-free part which is toxic to animals, whichever route of administration is used, when given in amounts of 0·19 gm. per kilo body-weight. It causes nausea, salivation, vomiting, passage of blood in the stools and vomit, convulsions and death. The alcoholic extract causes no more than a fall of arterial pressure which soon passes off. The volatile oil is a slight gastro-intestinal irritant, but the oily part of the seed is not poisonous, nor did the ether extract cause any symptoms. At autopsy there are signs of haemorrhage in the stomach and intestine (both small and large) and the mucosa is swollen and congested ; the liver is enlarged and congested with leucocytic infiltration, fatty degeneration and vacuolization of the cytoplasm, especially in the midzonal area, but also in the periportal and central. The kidneys are congested,

the convoluted tubules almost obliterated by the swelling of the lining cells ; the spleen is congested and may show haemorrhages ; the cerebral vessels are engorged [as would be expected in death after convulsions]. *H. Harold Scott.*

FAIR, G. M., CHANG, S. L., TAYLOR, Margery P. & WINEMAN, Margaret, A. **Destruction of Waterborne Cysts of *Entamoeba histolytica* by Synthetic Detergents.** *Amer. J. Pub. Health.* 1945, Mar., v. 35, No. 3, 228–32.

The authors have tested the cysticidal activity of a number of cationic, neutral and anionic synthetic detergents by exposing cysts of *Entamoeba histolytica* suspended in a quart of water to their action. After exposures of from 15 minutes to 2 hours, the cysts were washed and their viability tested by inoculating them to culture media. It was found that the cationic detergents were superior to the others. Thus the most successful were effective in one-third to one-fifth the concentration required for the neutral hexyl resorcinol, while the anionic detergents were not cysticidal in the concentrations tested. The successful detergents required a concentration ten times as great as that necessary for chlorine, which has been shown to be approximately 3 p.p.m., 2 p.p.m. and 1 p.p.m. for exposures of 15, 30 and 120 minutes respectively [this *Bulletin*, 1942, v. 39, 313 ; these are doses, not residual values]. One advantage of the detergents over chlorine is that the activity is not affected by the presence of organic matter in the water, while changes in hydrogen-ion concentration had little, if any, effect. A definite disadvantage is that water containing a detergent even in the minimal effective concentration tends to froth when shaken. Furthermore, there is a complete lack of information regarding any physiological effect the synthetic detergents may have on human beings. *C. M. Wenyon.*

RELAPSING FEVER AND OTHER SPIROCHAETOSES.

CHEN, Y. P., ZIA, S. H. & ANDERSON, H. H. **Immunity Reactions in Experimental Relapsing Fever.** *Amer. J. Trop. Med.* 1945, Mar., v. 25, No. 2, 115–16.

The authors infected two *rhesus* monkeys with a Californian tick-borne strain of *Spirochaeta recurrentis* by the intraperitoneal inoculation of blood from infected Chinese hamsters, in doses of 0·02 cc. per kilo.

Both monkeys showed spirochaetes in the peripheral blood 60 and 72 hours after inoculation and the blood remained positive for 24 to 36 hours. Seven days after the blood had become negative a second inoculation was given with double the initial dose, but neither spirochaetes nor febrile symptoms were noted, and a third inoculation also produced no obvious effects. Twenty-eight and 33 days after the disappearance of spirochaetes from the peripheral blood biopsies were performed and in both animals spirochaetes were found in the grey matter and blood-vessels of the brain.

Subsequently each monkey was inoculated with 2·0 cc. of blood from a patient infected with a Chinese, louse-borne strain of relapsing fever, but no spirochaetes were observed during a 31-day period of examination. Brain tissue removed from the monkeys at a second biopsy 50 and 54 days respectively after the first, showed no spirochaetes in the frontal lobe area.

Four Chinese grey hamsters, *Cricetulus griseus*, were splenectomized and inoculated with a Chinese strain of relapsing fever. Three of the four showed

spirochaetes in the peripheral blood 4 to 6 days later. After 23 days these hamsters were inoculated with the Californian strain and all showed spirochaetes in the blood, but for a short period only, in contrast to the 3 to 4 attacks seen in control animals. The brains of these hamsters contained spirochaetes.

Hamsters inoculated with brain tissue containing spirochaetes did not show any signs of infection and when inoculated with infected blood developed normal infections. There was no appreciable difference in the infectivity of hamster blood containing spirochaetes, which was mixed with brain tissue and kept for 22 hours in the ice box, and similar blood to which no brain tissue had been added.

These results support the view that residual infection plays an important rôle in the immunity which develops after an attack of relapsing fever. They also indicate that cross-immunity exists between infections with the Californian and Chinese strains of *Spirochaeta recurrentis*. *E. Hindle.*

May, W. K. C. **Relapsing Fever with Meningitic Manifestation. A Case Report.** *Chinese Med. J.* (Chengtu Edition). 1944, July, v. 62A, No. 4, 142–3.

"A fatal case of relapsing fever in Yunnan is reported. The meningitic manifestations were marked and abundant spirochaetes were recovered from the cerebrospinal fluid following repeated negative blood smears."

Schuhardt, V. T. & O'Bryan, B. E. **Effect of Intracranial Penicillin Therapy on Brain Involvement in Experimental Relapsing Fever.** *J. Bacteriology.* 1945, Mar., v. 49, No. 3, 312–13.

In a previous paper [this *Bulletin*, 1945, v. 42, 387] the authors reported that, in rats infected with *Spirochaeta recurrentis* (*novyi*), intraperitoneal injections of penicillin which would cure the blood infection and prevent the cerebral infection, failed to cure the cerebral infection. In the experiments here reported, combined intracranial and intraperitoneal injections of penicillin were used.

Seventeen rats, infected 12 to 40 days before, were divided into six groups containing 3, 3, 3, 3, 2, and 3 rats respectively. Each of the rats of Groups I, II and III received 1,000 units intracranially and 400 units every 3 hours for 48 hours intraperitoneally. Group I rats had a single intracranial injection, Group II had two intracranial injections of 500 units, and Group III had three intracranial injections of 333 units. Group IV rats received intracranial injections of buffer solution (penicillin diluent), the same dose of phenobarbital (for anaesthesia) as the test rats, and the same total dose (7,800 units) of penicillin as the test rats, in 17 intraperitoneal injections. The 2 rats of Group V had no phenobarbital and no intracranial injections, but they had the same amount of penicillin, in 17 intraperitoneal injections. Group VI rats were not treated.

Two days after the end of penicillin treatment the brains of the rats were emulsified and "passed to fresh rats"; those of the test rats caused no infection while the brains of the control rats did. It would appear, therefore, that intracranial injection of penicillin can cure the brain infection in experimental relapsing fever in white rats. *J. F. Corson.*

Kaplan, Dora. **Studies on the Cultivation of Borrelia Gallinarum.** [Summary of Thesis for the Degree of Ph.D.] 3 pp. [Submitted to the Senate of the Hebrew University, Jerusalem, July, 1944.]

The following medium was found satisfactory for the culture *in vitro* of *Borrelia* [*Spirochaeta*] *gallinarum*:—

A. Basic salt solution 1,000 cc.; proteose Difco peptone 4 gm.; dextrose 1 gm.; thioglycollic acid 0·1 gm.

B. Before inoculation add to 10 cc. of A, 1 cc. of fresh rabbit serum and 0·6 cc. of chicken red cells resuspended in an equal volume of basic salt solution.

Instead of adding the chicken red cells they may be haemolysed with 3 volumes of water and the supernatant fluid, after centrifugation, used instead of the red cells.

The basic salt solution has the following composition : NaCl 5, Na_2HPO_4 2·5, KH_2PO_4 0·25, $MgCl_2$ 0·3, $FeSO_4$ 0·0005, $MnSO_4$ 0·0005, and H_20 1000.

The spirochaetes were cultivated on this medium for more than 30 months and retained their virulence for at least 13 months ; at 16 months they were found to be avirulent but they still produced specific immunity in fowls, lasting for at least 7 months.

Various modifications, produced by adding substances to the medium, were tested and were found to promote growth of the spirochaetes in varying degrees.

J. F. Corson.

YAWS.

STAVAUX, R. Deux cas de pian avec lésions bilatérales d'hyperostose peri-orbitaire. [**Two Cases of Yaws with Bilateral Perioribital Hyperostosis.**] *Rec. Travaux Sci. Méd. Congo Belge.* 1945, Jan., No. 3, 177–81, 2 figs.

Two cases of yaws with very early development of osseous lesions, including the involvement of the orbital margins, are reported.

The first patient was an African girl, aged 12 years ; she had numerous small ulcers, more like ecthyma than yaws, on her right breast, and bony swellings in various parts of the body. The bones affected were the superior maxillary and malar bones, the bones of the forearm, the right scapula, right calcaneus, and right first metatarsal. The first sign of the disease appeared about 3 weeks before as a small tumour on the right breast, which ulcerated after 3 or 4 days ; about a week later her breast was covered with small ulcers and the bony swelling appeared about the same time. The facial swellings involved the orbital margins formed by the superior maxillary and malar bones of both sides, and on the left side the orbital part of the frontal bone also. Her face had a somewhat Mongolian appearance.

The second patient, seen in the same month, was an African woman, aged 45 ; she had characteristic yaws lesions on the skin of her left calf and bony swellings involving the orbital margins formed by the superior maxillary and malar bones ; the left clavicle, left scapula and the distal end of the right tibia also showed swellings.

Both patients were cured within 2 months with bismuth.

The author remarks on the rareness of such orbital lesions ; although his hospital dealt with over 2,000 new cases of yaws a year, he had never seen a similar case in nine years, nor had a case of goundou been met with. Another point of interest was the very early appearance of the bone lesions in the first patient.

J. F. Corson.

LEPROSY.

AUSTIN, C. J. **Central Leper Hospital Makogai, Fiji.** 19 pp., 21 figs. 1944, Nov. 28. Issued by the Information Office, Fiji.

This is a well-illustrated general account of the Makogai Leper Hospital, by its superintendent, Dr. Austin, which has been published by the Fiji Government. The hospital is situated on a beautiful island 3 miles by 2½, which contains

separate villages for patients of different races from Fiji, the Solomon, Cook and Gilbert Islands. A general hospital is well equipped and includes an X-ray apparatus. Missionary sisters superintend the nursing and train numerous native nurses. The able-bodied patients are employed on agriculture, fishing, building, etc., which reduces the cost of upkeep and enables the sufferers to earn money. Religious services, sports, concerts and other amenities are provided, and a New Zealand Leper Trust furnishes a comforts and Christmas Day fund. An increase in the Fijian patients from 352 in 1919 to 444 in 1943 is due to earlier admissions, for the early neural cases have greatly increased, but the lepromatous admissions have fallen from 32 to 0. In 1928 1,000 trees were raised from seed sent by B.E.L.R.A., which provide half the hydnocarpus oil used in treatment. On an average 40 patients have been discharged yearly, with only 10 per cent. of relapses during the last 10 years. Compulsory isolation is in force, and under the very favourable conditions provided for the inmates, it is considered to be a success. The Fiji Government have done well in publishing this report, which should stimulate leprosy institutions in other British colonies to emulate the Fiji example of humane and efficient control of the disease.

L. Rogers.

British Guiana. **Annual Report. Leprosy Hospital, Mahaica, 1944** [Wharton, L. H., Med. Supt.] M.S., 16 typed pp.

Dr. Wharton was confirmed as medical superintendent from the beginning of 1944 in succession to the late Dr. Rose. This report shows that the subordinate staff consists of 52 males and 21 females. Sanitary measures have reduced the incidence of flies and mosquitoes, improved bread has been supplied and the co-operative spirit and mental outlook of the patients have improved with the provision of employment for 200 of the patients and recreations, cinema, etc., with the help of a special committee. During the second half of the year, 6,830 children were examined and 22 early cases of leprosy were detected. It is hoped soon to be able to examine all contacts of patients in their homes. Treatment has followed the usual lines for 300 in-patients, 591 others attending clinics, out of a total of 995 patients, 356 of whom were in hospital. The medical board admitted 35 new cases and discharged 23 on parole. The deaths amounted to 34 (9·5 per cent.), 10 of these were from septic complications, 5 from chronic nephritis and 9 from senile or general debility. Most of the patients are Africans, East Indians, mixed and Portuguese, in that order of frequency ; the Portuguese numbered 24. The report closes with the statement that there has been definite progress during 1944 in the control of leprosy, both from the treatment and public health aspects. *L. Rogers.*

Hopkins, R. & Faget, G. H. **Recent Trends of Leprosy in the United States. Report of Seven Hundred Cases at the National Leprosarium.** *J. Amer. Med. Ass.* 1944, Dec. 9, v. 126, No. 15, 937–43, 1 chart.

This is an instructive analysis of the leprosy cases in the National Leprosarium from 1928 to 1944, during which period there were 723 admissions. The present data are compared with those of 1921 to 1928. A table of State admissions during the two periods shows a notable increase of admissions from Texas in the second period ; many of these were found to have been infected in Mexico. They now exceed those from Louisiana itself. California and Florida have the next largest number of endemic cases, and Florida, Illinois and New York had a number of new admissions, most of which were imported cases. The number in these States has remained fairly constant. The imported cases nearly all (221 out of a total of 303) came from Mexico, the Philippines, British West Indies and China. A great decline in the cases from Massachusetts and

from Minnesota is attributed to a rapid disappearance of the original foci of infection. The racial distribution shows 127 white and 52 Negro Americans, 212 Mexicans, 87 French Canadians in Louisiana, 52 Philippine Islanders, 89 other Europeans, 26 Chinese and 49 South and Central American out of a grand total of 723. It is of interest to note that a number of soldiers were infected during the Spanish American war and the two recent world-wars while on military duty in Cuba, the Philippines, etc., and more are expected to develop during the next few years. Age and sex incidence were very similar to those reported from other countries. The 723 cases are classed as :—Mixed type 49·9 per cent., lepromatous 39·1 per cent. and neural 11·0, and in addition in recent years 31 were returned as tuberculoid. Patients were reticent about disclosing family relationships and in only 147 was a family history obtained. Conjugal infections were very few. Occupation showed no special incidence. In such cases as gave a clear history regarding the initial lesion, macules were much the most commonly met with. Of serological tests, the Kolmer and Kahn reactions were the most reliable, and, as the changes in the serum reactions were closely correlated with changes in the clinical manifestations, leprosy is considered to produce positive reactions in the absence of syphilitic infection. The duration of cases of all types combined, from admission to death, averaged only 10·3 years. In neural cases it was 14·5 years, in mixed 10·6 years, and in lepromatous cases 9·3 years. Only one tuberculoid case was fatal, 18 years after onset. Of the 723 patients, 145 were discharged with disease arrested and only 16 relapsed. The proportions discharged of the different types were as follows : 90 of 155 neural ; 20 of 31 tuberculoid ; 19 of 329 mixed ; and 16 of 208 lepromatous. As is usual, most deaths occurred as the result of nephritis (55), tuberculosis (37) and leprosy (26) ; 17 were from asphyxia due to leprous laryngitis, out of a total of 190. [This paper contains a large amount of information and should be read in full by all interested in leprosy.] *L. Rogers.*

DHARMENDRA & SANTRA, I. **Epidemiological Leprosy Surveys in various Parts of India.** *Leprosy in India.* 1945, Jan., v. 17, No. 1, 2–22, 3 graphs.

In this article the surveys carried out by Santra in selected areas of almost all the provinces of India during 1942 -44 are considered as a whole. In all of them, except the Kangra Valley in the Punjab, nearly the whole population in the visited villages was examined and the cases found were mapped out ; the results, among about 5,000 people in each area, were recorded in earlier papers. The following are among the most important points brought out by the inquiries ; they are illustrated in the original by the tabulated data. Considerable variations in leprosy incidence were met with in the same province and in the same races in different provinces ; these are not easy to account for. The incidence varied between 0·17 in Cachar Hindus and 6·64 in Hill Cacharis, both in Assam, with an average incidence, among 74,727 persons examined, of 2·33 per cent. and an incidence of lepromatous cases of 0·1 to 0·96 per cent. The proportion of lepromatous to total cases was 16 per cent., but it varied in different areas between 5 and 62 per cent., and in three areas the percentage was higher than 24 per cent. This gives some measure of the proportion of infective cases which should be isolated. On the whole, but with exceptions, a high total incidence is associated with a high incidence among children and of lepromatous cases. A high total incidence is considered to be the best indication of the spread of the disease and the seriousness of the leprosy problem in any given area. The proportion of infected children varies greatly, but was always lower than in those over 15 years of age. As usual, more males suffered than females, but in the absence of trained lady workers the data are unreliable on account of the purdah system. In some areas leprosy cases are ostracized, or a custom prevails

of isolating advanced cases in their own homes or in huts outside villages, but no distinction is made between uninfective nerve and highly infective lepromatous cases. It is important to note that where such measures are customary a high lepromatous rate tends to be associated with a low gross incidence and a low child rate. This indicates that such measures help to control the number of infections taking place, and also that, with proper instruction regarding the type of cases requiring to be isolated, practical use might be made of the custom where it is in force. *L. Rogers.*

Leprosy in India. 1945, Jan., v. 17, No. 1, 32–8. **Report of the Leprosy Research Department, School of Tropical Medicine, Calcutta, for 1943.**

This report includes an account of epidemiological inquiries dealt with above, but the following additional points are of interest. Further work by Dharmendra on the isolation of the antigens from Hansen's bacillus which includes the separation of the active protein by extraction with chloroform—have been done without the use of heat, in the hope of obtaining a more specific substance ; but without success, for it still gave reactions in non-contacts in the little-affected Punjab plains, possibly owing to traces of chloroform not completely removed. The former methods of extraction have been applied in the case of the bacilli of Kedrowsky and of Stéfansky's rat leprosy organism. Four fractions, similar to those of Hansen's bacillus previously reported on, have been tested on leprosy patients. In the case of all three bacilli the polysaccharide fraction is inactive, while the acid-soluble fraction is active and antigenically similar in giving positive reactions in neural and negative reactions in lepromatous cases. On the other hand, while the nucleoprotein and alcohol-soluble protein of Hansen's bacillus act in the same way as the acid-soluble fraction, those of Kedrowsky's bacillus and of the rat leprosy bacillus give positive reactions in both types of leprosy, and therefore have no prognostic significance. It thus appears possible to isolate a fraction, the acid-soluble one, from some acid-fast bacilli other than that of Hansen, with a similar action in contacts and non-contacts as that of Hansen's bacillus itself. The fact that Kedrowsky's bacillus is easily grown will thus greatly simplify the production of an antigen of value in leprosy prognosis.

The therapeutic value of sulphanilamide derivatives has also been studied. The injection into bacteriologically positive leprosy lesions of two grains of the drug in 2 cc. of arachis oil had no effect on the bacilli. Owing to the difficulty of obtaining trichloracetic acid for local applications, a 1 in 5 dilution of carbolic acid, well shaken, has been used as a substitute. Similarly 1 per cent. thymol has been substituted for 4 per cent. creosote for addition to hydnocarpus oil used for injections. It has previously been reported that sulphapyridine and sulphanilamide have a bacteriological effect on rat leprosy bacilli *in vitro* ; it has now been found that these drugs are ineffective *in vivo*.

L. Rogers.

Balagangadharan, K. V. **Significance of Serum Reactions in Leprosy with particular reference to Kahn Test.** *Indian Med. Rec.* 1944, Dec., v. 64, No. 12, 325–30.

The author refers to opinions of Muir, Lloyd and Maithra that Kahn and Wassermann positive reactions in leprosy are due to complicating syphilis, and to more recent contrary opinions. He goes on to record the following personal experience in the Madras Presidency. Tests were carried out on 170 leprosy patients, in whom syphilis and allied conditions giving positive reactions were excluded, with the following results.

Type	L.3	L.2	L.1	N.1
Cases	40	45	55	30
Positive ...	57·5 per cent.	36 per cent.	22 per cent.	10 per cent.

He therefore concludes that the Kahn reactions are reliable in leprosy as well as in syphilis. *L. Rogers.*

KIRKALDY-WILLIS, W. H. **Sympathectomy in Leprosy.** *East African Med. J.* 1945, Mar., v. 22, No. 3, 88–90.

An African man, aged 40, had had a pricking sensation and burning pain all over his body for 18 months, pain in the wrists and hands for 12 months, numbness of the fingers of the right hand for less than 12 months, and a spreading ulcer on the outer side of his right foot, involving the little toe, for 3 months. He was gradually losing weight.

On admission he was wasted and anaemic (Hb. 70 per cent.) ; both hands and the whole left forearm were insensitive, the small muscles of both hands were wasted and paralysed, both thighs and legs showed loss of sensation, both knee-jerks and ankle-jerks were increased, and there were light-coloured patches on the front of the chest and abdomen. There was a deep necrotic ulcer, 2 × 4 inches in size, on the dorsum of the outer border of the right foot involving the little toe, the two distal phalanges of which were exposed and necrotic.

Operation.—Under spinal anaesthesia, the right superficial femoral artery was freed from its sheath for 2 inches in the lower part of the femoral triangle after dividing 2 or 3 small branches; the adventitia was injected with normal saline and removed by blunt dissection, and the media was then painted with absolute alcohol, the excess being washed off with saline. The artery contracted to about one-third of its normal diameter and its pulsation was much diminished. The sheath was sutured and the wound closed. The ulcer was then excised, disarticulation at the metatarso-cuboid joint was performed and the ulcer was dressed with iodoform in paraffin.

Four days later the ulcer showed red granulations, but an abscess appeared on the outer border of the left foot and was incised. Ten days later the ulcer was clean and red, the incision in the thigh had healed, and the incision on the left foot had almost healed. After another 8 weeks the ulcer had quite healed.

The author has no doubt that the operation on the femoral artery produced more rapid healing than would otherwise have occurred ; he observed that the right foot remained warmer than the left for about a month after the operation. *J. F. Corson.*

SAGHER, F. **Effect of Grenz Rays on Leprous Infiltrations. Report of an attempt to influence Leprous Infiltrations by Roentgen Rays of Long Wavelength.** *Arch. Dermat. & Syph.* 1944, Nov., v. 50, No. 5, 311–14, 2 figs.

The author points out that early trials of roentgen and radium rays in the treatment of leprous nodules were rather unfavourable and might cause severe damage to the surrounding skin and underlying organs. He has therefore tried the far less dangerous grenz rays in doses of 600 to 8,000 rk, in a single exposure or in several fractional exposures, in a total of 18 selected cutaneous areas, all of which showed numerous lepra bacilli before treatment. The recorded details of repeated exposures in two well-developed mixed cases show that only doses of 2,000 r. and upwards were effective, larger doses being

used in proportion to the amount of infiltration of the selected erythematous patches. After four months to one year the skin lesions became clinically free from symptoms, but the general course of the disease was not modified, although, when new cutaneous lesions appeared, almost all the irradiated areas were spared and the advance of the process halted abruptly at the border of the treated areas. Moreover, histological examinations showed that both the cellular infiltration and the number of Hansen's bacilli were greatly decreased in the treated areas as compared with the immediately surrounding unexposed skin lesions. The author therefore advises the use of grenz rays in the case of disfiguring lesions, especially those on the face. *L. Rogers.*

Zanetti, V. Lèpre et prophylaxie au Congo Belge. [**Leprosy and its Control in the Belgian Congo.**] *Rec. Travaux Sci. Méd. Congo Belge.* 1945, Jan., No. 3, 96–108.

This paper gives a long general account of a system of agricultural village isolation of lepers (V.A.I.L. for short) in the Belgian Congo. Total compulsory segregation is not advised, for the estimated 60,000 cases, but numerous agricultural villages are being organized, each to provide for 300–400 cases, visited once or twice a week by a medical officer and with work for the able-bodied to reduce the cost and to provide food. A plantation of hydnocarpus trees in each will furnish the oil for treatment. Indirect and mild pressure is used to obtain admission of infective cases. Only uninfective patients are allowed to visit their homes, but visitors can come to the boundaries to see their relatives. The isolation is more or less voluntary in most cases and the cost is moderate. All possible social amenities are provided. A home is provided for the healthy children of patients. The original diagnosis, and examinations before discharge when the disease is arrested, are always made by doctors, with bacteriological tests. In treatment a mixture of hydnocarpus oil and sodium gynocardate is much used. *L. Rogers.*

Delperdange, G. Sur la présence probable du bacille de Stephansky à Coquilhatville. [**The Probable Presence of Rat Leprosy in Coquilhatville.**] *Rec. Travaux Sci. Méd. Congo Belge.* 1945, Jan., No. 3, 109–11.

This note reports that acid-fast bacilli were found in 52 of 470 rats examined (9 per cent.). One showed lesions of the skin, internal organs and glands, containing very numerous acid-fast bacilli and microscopical changes characteristic of rat leprosy. An inoculated white rat developed similar lesions after several months, but attempts at cultivating the bacilli have been negative. Guineapigs were negative to inoculation and so was a monkey at the time of reporting. The author concludes that it is probable that rat leprosy occurs in the Belgian Congo, but further work is required to establish this.

L. Rogers.

HELMINTHIASIS.

Kuo, Shao-chou & Kiang, Liu-mei. **The Animal Parasites of Dogs in Chengtu.** *Chinese Med. J.* (Chengtu Edition). 1943, Oct., v. 62A, No. 1, 15–18.

E. C. Faust in 1929 reported his results from an investigation of the animal parasites of dogs and cats in China ; H. T. Chen studied in 1934 the helminths of dogs in Canton [this *Bulletin*, 1935, v. 32, 620] ; T. H. Chin and K. C. Li the

parasites of dogs and cats in Kweiyang [*ibid.*, 1943, v. 40, 847], and the same authors with K. CHANG and W. K. TONG ankylostomiasis in Szechwan [*ibid.*, p. 851].

The authors of the present paper examined carefully 40 stray dogs caught in the streets of Chengtu. They found ectoparasites of: *Ctenocephalus felis* and *Pulex irritans*; *Trichodectus canis*; species of *Amblyomma* and *Haemaphysalis*, and *Hippoboscus*.

The helminthic parasites were of much interest; all 40 showed some helminthic infestation. Thirty-six were harbouring *Ancylostoma caninum*, on an average less than 20 per dog, but one had 73. *A. braziliense*, which has been reported in Chengtu, was not found among these. *Toxocara canis* was found in 12, but in one only (which contained 15) was the number over 10; *Dirofilaria immitis* was present in the hearts of four, in large numbers, and in one there were three specimens of *Spirocerca sanguinolenta* in an oesophageal tumour. Twenty-four of the 40 were infested with *Dipylidium caninum*, one had as many as 143; eight harboured *Diphyllobothrium mansoni*, but no case of human sparganosis has been recorded in Chengtu. *Taenia* [species not stated] in two; five specimens of *Echinococcus granulosus* were found in one dog, the only one of the 40 found thus infested. *Metagonimus yokogawai* was found in seven, but only one was heavily infested (172 specimens); *Echinochasmus perfoliatus* in two and *Paragonimus* sp. in one (four flukes being present). *Clonorchis sinensis*, common in cats, was not seen in any of the 40 dogs.

It is noted that corn-sweet-potato growers in Northern Szechwan suffer severely from ground-itch and that dogs' faeces are used frequently as fertilizer; it would be interesting to examine the local inhabitants, especially the agricultural workers, for infestation by *Ancylostoma caninum*.

H. Harold Scott.

ANDREASEN, A. T. & SURI, H. L. **A Case of Schistosomiasis Infection contracted in India.** *Indian Med. Gaz.* 1945, Feb., v. 80, No. 2, 93–4.

This appears to be the first recorded case of infestation with *Schistosoma haematobium* having been acquired in India.

A Sepoy, aged 19, with four months' military service, was admitted to hospital at Rawalpindi, Punjab, suffering from haematuria which was thought to have been due to an injury received while playing hockey a fortnight before. Ova of *S. haematobium* were found in his urine and on cystoscopic examination the bladder had the typical appearance of schistosomiasis. No evidence of intestinal schistosomiasis was found.

The patient was said not to have been outside his native district of Ropar, Ambala, Punjab, except for a short visit to Poona and his military posting to Rawalpindi. As the disease was well established it is thought probable that he contracted it in his native village of Talapur, and that intermediate snail hosts must exist there (possibly at Poona); it had not yet been possible to investigate this.

The authors mention the obvious importance of this case in view of the movements of troops between India and countries where the disease exists.

J. F. Corson.

BARNETT, L. **Hydatid Incidence in New Zealand for the Year 1943.** *New Zealand Med. J.* 1945, Apr., v. 44, No. 240, 99–100.

WAR OFFICE. ARMY MED. DEPT. BULL. No. 47, 1945, May, 2–3. **Ancylostomiasis complicating other Disease—A Reminder.**

"Doctors, both service and civilian, are not perhaps aware how often white troops may have hookworm ova in the stools after service in an area where

infection is common among the native population. Symptoms are uncommon and infection may not become apparent unless the men are investigated in hospital for some other disease. Relapsing malaria, especially in personnel returning from the Far East, may be complicated by infection with one of the varieties of ancylostoma. An eosinophilia of more than 5 per cent. is suggestive of infection and a haemoglobin of less than 80 per cent. may be due to a long-standing and heavy infection ; in either case examination of the stools should be made.

" In an Australian General Hospital an investigation was made to find out the frequency of hookworm infection among white troops.[1] Stools and blood of 2,000 patients were examined ; about 1,600 of these had served in New Guinea for periods varying from a few weeks to 18 months. Eight hundred men were excreting hookworm ova ; laboratory culture of the ova from the faeces of a small sample of the group showed that half were infected with both *Ancylostoma duodenale* and *Necator americanus*. In most the infection appeared to be light and it was estimated that they had less than 20 female worms in their intestines. Different brigades showed varying infection rates ; in one unit it was 97 per cent.

" A history of ' ground itch ' or ' creeping eruption '[2] was not obtained from the patients ; this is surprising as the commonest mode of entry of the hookworm is through the hair follicles of the legs ; this may follow marching through infected swamps. The ingestion of infected drinking water or uncooked vegetables is a less common route of infection ; many of the men gave a history of vague dyspepsia during their service in New Guinea. In addition to ova, occult blood was often found in the stools. Eosinophilia was variable, diminishing with successful treatment.

" Different methods of treatment were tried. It was confirmed that two drugs in combination gave better results than either used alone. In the British Army[3] this has also been the experience and it is advised that tetrachlorethylene should be used in combination with oil of chenopodium. The drugs are mixed together, 4 c.c. of tetrachlorethylene and 1 c.c. of oil of chenopodium ; this draught is given in the early morning on an empty stomach, no food being allowed until the bowels have been satisfactorily moved ; if necessary this may be assisted with a dose of epsom salts a few hours later.

" The effects of treatment may be judged by the number of ova found in the stools, the degree of eosinophilia, and the cessation of symptoms if these have been present. In about a quarter of the cases two or more courses are required to eliminate all worms, but it should seldom be necessary to hospitalise men for more than a few days on account of uncomplicated ancylostomiasis. The finding of an occasional ovum is no justification for retention in hospital.

" It is always wise to consider ancylostomiasis as a cause of uncomplicated anaemia. A heavy infection may cause a considerable degree of anaemia resistant to treatment until the infection has been eliminated."

TANG, W. K. & CHANG, K. **Symptoms of Hookworm Disease.** Reprinted from *Chinese Med. J.* (Chengtu Edition). 1943, Oct., v. 61A, 105–6.

This is a short note of the symptoms found in 44 patients severely infected by hookworms (*A. duodenale* and *N. americanus*) in Szechwan ; for their information, the authors relied largely on the patients' own statements. The most common complaints were :—ground itch, cough, intestinal discomfort, diarrhoea alternating with constipation, geophagy, cardiac palpitation, tinnitus, and

[1] *Unpublished report.* 1945, RFA (45) 3, Australian Army Staff, London.
[2] This *Bulletin*, 1944, Oct., No. 40, article 312.
[3] *Memoranda on Medical Diseases in Tropical and Sub-Tropical Areas.* War Office, 1942, page 10.

muscular weakness. The cough was sometimes associated with asthmatic symptoms, started 2–10 days after the appearance of ground itch, and lasted for 2–3 months. [In a patient with such a history, a sputum examination for tubercle bacilli would be advisable.] There was no definite relation between intensity of infection and haemoglobin percentage, but the haemoglobin values of these patients were very low. [Much modern work indicates that symptoms of hookworm disease are unlikely to appear unless there is some degree of malnutrition. If this is so, it seems possible that some of the symptoms noted above may have a nutritional, as well as a hookworm basis.] *Charles Wilcocks.*

CHANG, K. & CH'IN, H. T. **An Evaluation of Pickled Vegetables in the Dissemination of** *Ascaris lumbricoides.* Reprinted from *Chinese Med. J.* 1943, Jan., v. 61A, 63–9, 2 figs.

Infection with *Ascaris lumbricoides* is very common in the Province of Szechwan ; the incidence varies from 86 to 95 per cent. and it is estimated that the average worm burden is about 20, though estimates of over 100 are not uncommon. The authors decided to investigate the possibility that vegetables, grown in soil fertilized with human faeces, and pickled in brine to which are added wine and sugar, might contribute to the spread of infection. The process of pickling, which is essentially one of bacterial fermentation, is described, and it is stated that vegetables pickled in this way form a very large item in the daily diet of the people.

Three methods of examination were used. In the first, brine from the jars containing the pickled vegetables was centrifuged, and the sediment was either examined microscopically, or was subjected to floatation techniques to pick out the eggs. In the second, washings of the pickled vegetables were examined. In the third, tests were made of the viability of eggs collected from the faeces of children and kept in brine, by observing the embryonation of eggs which were undeveloped at the beginning of the experiment, or the vacuolization of embryonated eggs and the activity of the larvae.

The first method revealed 7·14 per cent. of positive results in 378 specimens from houses or condiment shops ; most of the *Ascaris* ova were apparently viable. The floatation techniques were not useful. The second method was a failure. The third method showed that a large proportion of eggs, kept in brine at room temperature for 30 days, remained viable, whether originally undeveloped or embryonated.

Details of the findings are given, and the conclusion is reached that pickled vegetables are able to play a part in the spread of *Ascaris* infection, though "in rural communities there are other more important sources which are responsible for more widespread and heavy infections in West China." The authors also quote from their own unpublished work, in which they found that 17·5 per cent. of the [presumably fresh] vegetables on Chengtu markets were contaminated with *Ascaris* eggs. *Charles Wilcocks.*

CHANG, K., TONG, W. K., CHIN, H. T. & LI, C. H. **Quantitative Studies on** *Ascaris lumbricoides* **in Szechwan.** Reprinted from *Chinese Med. J.* 1943, July, v. 61A, 166–9.

In this short note the authors record the findings relating to infection with *Ascaris lumbricoides*, made during a hookworm investigation in Szechwan. Examination was made by the smear, the Willis and the Stoll technique, and the result indicated infestation in probably 100 per cent. of the inhabitants of certain regions. Children were usually heavily infested, but some adults also had numerous worms. The average *Ascaris* burden for children was 27 ; for

all ages 17, but burdens of 150 or more were found. [These seem to be calculated on the number of eggs passed.] Details are given of the findings in various areas. *Charles Wilcocks.*

UNGAR, H. **Complications due to Ascariasis, as observed at Autopsy.** *Harefuah.* Jerusalem. 1945, June 1, v. 28, No. 11. [In Hebrew 237–40, 5 figs. English summary 240–41.]

" Post-mortem findings in eight cases of ascariasis are reported. In six, the fatal outcome was directly influenced by the presence of worms. The cases illustrate different ways in which ascaris may be the cause of serious complications. There were three cases of intestinal obstruction with subsequent gangrene of the intestinal wall, one case of invasion of worms into the common bile duct and one into the pancreatic duct, and three cases of toxic damage to the intestinal wall, probably caused by substances produced by the disintegration of dead worms.

" All cases but one support the opinion expressed by some authors that serious complications depend not so much on the presence of excessive numbers of worms in the intestines but rather on the coincidence of other pathologic factors which may be summarized as follows :

" (1) Obstruction may occur as a result of spasmodic contractions of the intestinal wall around groups of worms because of increased peristalsis during febrile diseases, acute enteritis, amebic dysentery (case 1), reversible torsion due to congenital malformation (case 2), transient interference with the secretion of bile caused by calculi or worms (case 3).

" (2) Invasion of the bile or pancreatic ducts is more likely to take place when the sphincter of the papilla of Vater has become inefficient during chronic inflammation (case 4) or in cases of anomalous fusion of the pancreatic and common bile ducts at some distance from the papilla (case 5). Achylia gastrica is considered as a subsidiary factor which enables worms to migrate from their usual site in the jejunum in the direction of the esophagus. It should be mentioned that the diagnosis of worms in the papilla may be confused with the diagnosis of passing gall stones. If worms do not return to the intestinal lumen as may be assumed in case 2, a later sequel of the invasion of worms into the biliary ducts is suppurative cholangitis with the formation of multiple abscesses in the liver (case 4).

" (3) Lesions of the lungs in ascariasis are of two kinds. Severe hemorrhages into the lungs have been observed in the course of the developmental cycle of ascaris during its passage through the pulmonary capillaries (case 2). In an indirect way, damage may be done to the lungs when the presence of ascaris in the stomach induces vomiting and the vomitus is aspirated into the respiratory organs (case 8). The importance of this finding for the development of post-operative pneumonia has been stressed by some surgeons.

" (4) Severe lesions of the intestinal wall have been noted in two cases where macerated worms were found in the lumen.

" Case 7 was that of a young diabetic who was admitted in coma. In spite of adequate anti-diabetic treatment the patient died within 24 hours after admission. Death was caused by peritonitis which started from a necrotic segment of the ileum. The same segment contained groups of dead worms.

" Case 8 deserves special attention even in a short review of the original article. A woman aged 28, died 11 days after a gastric resection had been performed for duodenal ulcer. For about 8 days following the operation, the recovery was uneventful. Then, the patient vomited several worms and afterwards developed signs of bronchopneumonia. Towards the end there was evidence of severe hemorrhage into the intestinal tract.

" Necropsy revealed the stomach and duodenal stump filled with dead worms in a state of advanced decomposition. In the duodenum they were enclosed in soft blood clots which covered two round perforations with thin ' punched-out ' margins. There was a small amount of blood in the subhepatic area of the peritoneal cavity, but no evidence of acute peritonitis. From macroscopic and microscopic examination, the conclusion seemed justified that acute perforation was a sequel to necrosis of the duodenal wall due to the action of toxic substances liberated from the body of dead ascaris."

VINNITZKY, I. M. **A Comparative Study of the Defensive Reaction of the Organism of various Animal Species to parenterally introduced Living Nematodes.** *C. R. (Doklady) Acad. Sci. URSS.* Moscow. 1944, v. 45, No. 4, 173–6. [In English.]

Using guineapigs, rabbits, cats, dogs and hens, the author surgically introduced into the peritoneal cavity either living or dead " *Ascaris suum* " (*Ascaris lumbricoides*) and *Toxocara canis* and studied the histological reactions of these animals. [He does not state whether both these nematodes were introduced into all these animals. He does not discuss the fact that the animals used are all unusual hosts for *A. lumbricoides* and that only the dog and cat are normal hosts for *T. canis*. It is well known that the reactions of unusual hosts are more vigorous than those of normal hosts. The author does not mention the work of CHANDLER (this *Bulletin*, 1937, v. 34, 39), who surgically implanted dead *Nippostrongylus muris* of the rat into the body cavity of laboratory rats, and adult *N. muris* into the intestine of rats (*ibid.*, 1936, v. 33, 588), and also (*ibid.*, 1936, v. 33, 120) surgically united the circulations of two rats infested with this species. Chandler's results show that work of this kind should compare the results obtained in normal and abnormal hosts and also those obtained with species whose larvae migrate through the body of the host, whether they penetrate the skin (*Nippostrongylus*) or not (*e.g.* Ascaroidea) and those whose larvae do not thus migrate.]

Vinnitzky found that the introduction of even large numbers of *A. lumbricoides* and *T. canis* did not, so long as the nematodes were alive, cause any important clinical symptoms in the cats, dogs and guineapigs ; but when the nematodes were first killed, the experimental animals died, and when they were first " dissected," so that the perienteric fluid was liberated into the experimental animal, the death of the latter was very rapid. If, however, the animals were first immunized by previous introduction [presumably surgical introduction] of living ascarids, they resisted repeated introductions of dead or " dissected " ones.

The two species of nematodes used lived in the animals for varying periods up to 10–12 days. They showed a tendency to leave their unaccustomed situation ; they were able to bore into the intestinal lumen and in one instance perforated the stomach wall. Microscopical examination revealed blood in the intestine of ascarids living in the peritoneal cavity. In guineapigs the parasites were encapsuled, and phagocytosis followed, first by polymorphonuclear microphages and later by mononuclear macrophages, both of which can penetrate the nematode cuticle and egg membrane. Probably these cells also secrete enzymes which help the process. Phagocytosis was at its maximum 33–35 days after the operation. In guineapigs killed 57–62 days after it there was no trace of the parasites. In rabbits there was early encapsulation and multiple adhesions [" coalescences "] of the abdominal organs. An overabundant " exudation " of leucocytes slows up or completely stops the phagocytosis ; the ascarids are walled off by leucocytes, but penetration into the cuticle, eggs or other organs of the nematodes was never seen. The nuclei of

the leucocytes showed karyolysis and karyorrhexis, and, round the ascarids, they were converted into a necrotic mass, in which, 47 days after the operation, the ascarids and their eggs were still intact.

In dogs and cats there was no encapsulation, but very rapid lysis of the ascarids, the rate of which varied with the number of nematodes introduced, and with the response of individual animals. Usually lysis of 2–3 living ascarids was complete in 9–12 days. Into one cat, weighing 2,800 gm., 31 *A. lumbricoides* measuring 20–30 cm. long were introduced and at autopsy, 42 days after the operation, complete lysis had occurred. During the lysis and soon after its completion, the peritoneal fluid of the cats contained large numbers of neutrophil polymorphs and " monocytoid " cells and cells transitional to very large and active polymorphonuclear macrophages. Polymorphonuclear cells penetrated the ascarid cuticle, and later the internal organs, and also destroyed the eggs. No adhesions of abdominal organs were seen in carnivora. In hens there was no lysis and no phagocytosis ; the ascarids were " simply mummified."

Thus the process was essentially the same in all the experimental animals and the author relates it to what happens in the normal life history of various nematodes, *e.g.*, when nematodes leave the intestine, when the development of their migratory larvae is prevented by encapsulation, when encapsulation is a necessary phase in the life history or when mature species live normally in the peritoneal cavity and are encapsuled only when they are dead or dying. The response observed is essentially the same as that shown to a foreign body and to pathogenic agents in general, namely immigration of phagocytes, proliferation of connective tissue and encapsulation and, after the isolation of the parasite, destruction of it by phagocytosis. If it cannot be destroyed, the host either succumbs or host-parasite adaptation develops in the course of evolution. Cats and dogs have, however, developed the ability to destroy these parasites. The author explains this by the view that, in most animals, encapsulation precedes phagocytosis or occurs simultaneously with it, so that phagocytosis is greatly delayed or prevented ; but in carnivora the phagocytes have a maximum mobility and activity, while encapsulation is delayed or eliminated. Probably this is not a special defensive reaction developed by carnivores to nematodes ; it is more likely that, in the course of evolution, the mesenchyme of carnivores has developed a phagocytic response which is more efficient than that of other animals. *G. Lapage.*

Yu, N. G. & Mao, C. P. **Preliminary Report of *Microfilaria malayi* Infection in Chungking.** *Chinese Med. J.* (Chengtu Edition). 1944, Apr., v. 62A, No. 3, 114–20, 2 charts. [18 refs.]

A Chinese man, aged 18, was admitted to Chungking Municipal Hospital, Szechwan Province, in October, 1943, because microfilariae had been found in his blood about two weeks before by a malaria unit. Observations on morphology and periodicity were made and are recorded in tables. It was impossible to determine when and where he became infected, but he is stated to have lived in the neighbouring province of Hupeh for the first 11 years of his life, *i.e.*, until 1936, since then in Szechwan province, and never to have been to other provinces. The microfilariae were most numerous at night, reaching the maximum at 2 a.m. *J. F. Corson.*

Brady, F. J., Lawton, A. H., Cowie, D. B., Andrews, H. L., Ness, A. T. & Ogden, G. E. **Localization of Trivalent Radioactive Antimony following Intravenous Administration to Dogs infected with *Dirofilaria immitis*.** *Amer. J. Trop. Med.* 1945, Mar., v. 25, No. 2, 103–7, 2 figs.

Culbertson & Rose [this *Bulletin*, 1944, v. 41, 772 ; 1945, v. 42, 136] used cotton rats infected with *Litomosoides carinii* in chemotherapeutic tests

on filariasis with antimony compounds. This element is difficult to detect in small amount in tissues and fluids. GOODWIN and PAGE [this *Bulletin*, 1944, v. 41, 20, 222] have studied its excretion in laboratory animals, using a polarographic method. The present investigation deals with the distribution and fate of injected antimony compounds in dogs and it is hoped that the methods may serve as an aid in selecting new chemotherapeutic agents. After trying biological and spectrographic methods, without success, radioactive antimony prepared with the aid of the cyclotron was employed. A technique was developed for locating the active substance in tissues by mounting thin sections on a photographic plate. Radioactive phosphorus had previously been used by MCCOY *et al.* (*J. Parasitol. Supplement* 1939, v. 25, 33; 1941, v. 27, 53) in studies on encysted *Trichinella* larvae. The radioactive antimony was obtained as the trioxide and was then used in synthesis of tartar emetic and sodium antimonyl xylitol. The degree of radioactivity in compounds and tissues was determined by means of Geiger-Mueller counters with scaling circuits and also by the ionization chamber. Four dogs naturally infected with *Dirofilaria immitis* were treated intravenously with the three compounds and received 0·8 mgm. of antimony per kilo. of body weight. Blood and urine were then collected at intervals up to 36 hours, when the animals were killed and residual urine and tissues were collected for determination of their radioactivity by comparison with standards. In the range 0·25–40 micrograms the accuracy of determination was very high. It was found that nearly all injected antimony had left the blood in a few hours. The liver contained the greatest concentration and next in order of content came the thyroid tissues. The adult worm on recovery contained about $\frac{1}{7}$ that in the liver. The lymph nodes and dermis, which are the chief sites of some adult human worms, contained very little antimony. After 36 hours the amount excreted in the urine varied from 10 to 20 per cent. of that injected. The fluid and tissue content of the element after injection of the insoluble trioxide was low. *J. D. Fulton.*

FRANCISCO RUIZ R. Datos para la exploración clínica del oncocercoso. [**Clinical Findings in Onchocerciasis.**] *Bol. Oficina Sanitaria Panamericana.* 1944, Dec., v. 23, No. 12, 1081–9. English summary.

Onchocerciasis, common in Africa, west and east, but especially the former, is found in the New World only in Guatemala and Mexico, and in the latter of these in the States of Chiapas mainly, and, to a less extent, in Oaxaca.

This article is a general talk on the disease from the clinical aspect, a sort of clinical lecture to students, telling them what questions to ask a patient regarding the history, place of residence, habits, occupation; what signs to look for, such as tumours, eye lesions, laboratory examinations for eosinophilia and for filarial embryos in the skin. It contains nothing which is not familiar to readers of this *Bulletin.* *H. Harold Scott.*

DEFICIENCY DISEASES.

GILLMAN, T. & GILLMAN, J. **Methionine and the Fatty Liver of Infant Pellagrins.** [Correspondence.] *Nature.* 1945, May 26, 634.

The authors have already described the syndrome of malignant infantile pellagra in South African children, and the dramatic cure which may be attained by treatment with ventriculin, even when treatment with nicotinic acid or other vitamins has been unsuccessful [see this *Bulletin*, 1944, v. 41, 1057]. One of

the most important features of this disease, and one which gave the best criterion of the condition, was the presence in the liver cells of large amounts of fat, and the authors have devised an improved method of liver biopsy by means of which the progress of the disease can be studied. They tested the effect of methionine in two infants exhibiting the syndrome of malignant pellagra, while a third infant, with the same condition, was studied as a control [it is known that small quantities of methionine decrease the liver fat content]. The condition of the liver at the beginning of treatment was similar in all three.

The infants were given maize porridge and half strength milk, and methionine was administered orally—8 gm. in four days and 11 gm. in seven days in the two infants respectively—but had no beneficial effect. It was then stopped and treatment with ventriculin and a full diet was substituted ; recovery took place, but was slow. The control infant received no treatment at first, and was given the same porridge and milk, but when ventriculin was administered, rapid and uneventful recovery took place.

Under fluorescence microscopy, there was no typical vitamin A fluorescence in the Kupffer cells, but the fat droplets in the liver cells showed a dull greenish-white fluorescence ; this does not imply that they will respond to methionine. It is evident that, under these conditions, methionine is not useful ; the best treatment remains the administration of ventriculin and a full diet.

Charles Wilcocks.

Pitão, J. S. Deficiência de ácido nicotinico em patologia humana (pelagra). [**Nicotinic Acid Deficiency in Pellagra.**] *Brasil-Medico.* 1945, Jan. 6 & 13, v. 19, No. 1 & 2, 4–13, 7 figs. [30 refs.]

Copping, A. M. **Some Aspects of Riboflavin Nutrition in Man.** *Nutrition Abstracts and Reviews.* 1945, Jan., v. 14, No. 3, 433–40. [80 refs.]

A review of the literature, which does not lend itself to abstraction. Most of the papers referred to have been reviewed in this *Bulletin.*

SPRUE.

Isbister, J. **A Case of Sprue Syndrome.** *Med. J. Australia.* 1945, Apr. 14, v. 1, No. 15, 371–4, 4 figs. [15 refs.]

This is a full and well documented account of a classical case of tropical sprue in a man of 32 from Cairns, Queensland. The diagnosis was made on the following points :—(*a*) general asthenia and emaciation ; (*b*) ulceration of the mouth ; (*c*) fatty diarrhoea ; (*d*) macrocytic anaemia ; (*e*) flat curve result of the oral glucose tolerance test ; (*f*) deficiency pattern of the small intestine ; and (*g*) course of the disease.

Special attention has been paid to the radiographic appearances of the small intestine. The *moulage* sign in the upper jejunum is so called because the opaque meal has the appearance of wax poured into a mould. This finding is diagnostic of steatorrhoea. Dilatation is present and segmentation in the more distal portions of the small intestine is shown by the clumping together of the barium in separate areas ; it is probably due to spasm. *P. Manson-Bahr.*

HAEMATOLOGY.

TAYLOR, G. F. & CHHUTTANI, P. N. **Nutritional Macrocytic Anaemia and the Animal Protein of Diet.** *Brit. Med. J.* 1945, June 9, 800–802.

Fifty consecutive unselected cases of anaemia were admitted to a hospital located in a hot, desert climate, serving a population of adult male Indians, of whom 17,000 were meat-eaters and 1,188 vegetarians. The admission rate per 1,000 for anaemia was 22 times as great among the vegetarians as among the meat-eaters.

The anaemia also differed in type and severity in the two groups, being mainly severe and macrocytic in the vegetarians but mild and hypochromic in the meat-eating group. No case of nutritional macrocytic anaemia was seen in a meat-eater, while 24 cases of nutritional macrocytic anaemia occurred amongst the vegetarians.

Vegetarianism was thus thought to be the principal cause of nutritional macrocytic anaemia in this series. *L. J. Davis.*

DERMATOLOGY AND FUNGOUS DISEASES.

LEÓN-BLANCO, F. & OTEIZA, A. **The Experimental Transmission of Pinta, Mal del Pinto or Carate to the Rabbit.** *Science.* 1945, Mar. 23, 309–11.

In Cuba one of the difficulties of studying mal del pinto is that pinta-like lesions can be produced by the spirochaete of syphilis. Several investigators have tried to infect laboratory animals with *Sp. herrejoni*, the causal agent of pinta, but with equivocal success. The importance, therefore, of this contribution is great.

A Jamaican negress showing the signs of pinta on palms and soles was seen by the authors and the organism was visible in material from the lesions. But this organism is not distinguishable morphologically from that of syphilis, and the Kahn and Meinicke reactions are positive in both. To prove that the condition was pinta and not syphilis, a volunteer was inoculated at two points on the front of the left forearm with fluid from the lesions. Primary pinta manifestations appeared here in course of time and there were, when writing, signs of general spread of pintids. Forty-five days after the primary inoculation of the volunteer, serous fluid squeezed from the initial lesion (which contained the spirochaetes) was diluted with normal saline and four rabbits were inoculated intradermally in the scrotum. Fifteen weeks later one of them presented a pink papule at the inoculation site, which in another ten days became an erosion covered by a scab. From the base of this a bloody serum oozed, containing numerous spirochaetes, and four more rabbits were similarly inoculated from this. No lesions have as yet developed in these [the interval is not stated, but from information gleaned from the text, probably 54 days], but a volunteer inoculated at the same time as this second batch of rabbits developed a local inflammation which cleared in 72 hours ; but 13 days after the inoculation an erythema, 2 mm. in diameter, was seen which ten days later became an infiltrated papule and in another month measured 6 by 4 mm. and had a fine scaly surface and many spirochaetes were seen in the expressed fluid. " In the present state of our knowledge the only laboratory method which will allow with certainty to differentiate syphilis from pinta, mal del pinto or carate, is the experimental inoculation of man, with the production of an initial pinta lesion

different from that of syphilis and pian." [A method not altogether devoid of risk in a country where syphilitic lesions may simulate those of pinta.]

H. Harold Scott.

Clough, F. E. **Madura Foot.** *Western J. Surgery, Obstet. & Gynecol.* 1945, May, v. 53, No. 5, 153–6, 3 figs.

A report of a case.

HEAT STROKE AND ALLIED CONDITIONS.

Eichna, L. W., Bean, W. B., Ashe, W. F. & Nelson, N. **Performance in relation to Environmental Temperature, Reactions of Normal Young Men to Hot, Humid (Simulated Jungle) Environment.** *Bull. Johns Hopkins Hosp.* 1945, Jan., v. 76, No. 1, 25–58, 19 charts. [16 refs.]

The physiological reactions were studied of 64 healthy young men who lived continuously in a hot room for periods of 8–32 days. During the day the men were exposed to an environment having a dry bulb temperature of 90°F. with a relative humidity of about 95 per cent. At night the temperature was lowered to 85°F. and the relative humidity to 75–80 per cent.

If the men were given progressively increasing work, acclimatization to the heat was apparent on the second day of exposure and was complete in seven to ten days. Acclimatization resulted in the men being able to work with a lower heart rate, lower skin and rectal temperature, a more stable blood pressure and less discomfort than on the first day of exposure to the heat. Men resting in the heat for six to ten days achieved only a small degree of acclimatization as measured by their ability to work in the heat. Physically fit men were found to acclimatize more rapidly than unfit men and when acclimatized were capable of more efficient work. Initial intolerance to heat did not preclude rapid and complete acclimatization if adequate rest, water and salt was provided. A considerable degree of cross acclimatization between desert and hot humid climates was demonstrated.

Adequate water intake was found to be the most important factor influencing the performance of acclimatized men in the heat, with physical fitness next in importance ; but it should be pointed out that the effects of restricting the salt intake, the effects of varying the severity of the work, or of varying air movement were not studied. Restricting the water intake of acclimatized working men led to a marked deterioration in performance without reducing the rate of sweating. Clothing was found to increase the strain imposed by the hot humid environment though the deleterious effect was somewhat less if the clothing was wet. Other factors mentioned as adversely affecting performance in hot humid environments were inadequate sleep, the taking of alcohol, and long periods of work, but no satisfactory data are presented concerning these points. Small changes in environmental temperature were found to have a marked effect on the physiological response.

One group of four men working in the humid heat during a continuous stay of 23 days developed a definite deterioration in performance after reaching the peak of their acclimatization. Their performance on returning to the heat, after four days in cool conditions, was as good as at the peak of acclimatization. An attempt to achieve a similar deterioration in 15 men who worked in the humid heat during a stay of 28 consecutive days resulted in failure.

The authors stress that sweating in humid heat is profuse, grossly inefficient, wastes water and salt, and is independent of fluid intake. Replacement of lost

water and salt is essential, but they point out that thirst is a lagging guide to these needs.

A considerable number of charts illustrate the various points, but no tables of results are given. *B. McArdle.*

BURCH, G. E. **A Method for measuring Small Amounts of Weight Loss in Man.** *Amer. J. Med. Sci.* 1945, Feb., v. 209, No. 2, 220–26, 3 figs.

A balance is described by which a human subject can be weighed with an accuracy of 0·150 gm. Changes of weight can be recorded photographically over short or long periods. *J. Waterlow.*

BURCH, G. E. & WINSOR, T. **The Relation of Total Insensible Loss of Weight to Water Loss from the Skin and Lungs of Human Subjects in a Subtropical Climate.** *Amer. J. Med. Sci.* 1945, Feb., v. 209, No. 2, 226–34, 1 fig. [11 refs.]

By means of the balance described, measurements of insensible weight loss were made in normal human subjects. The room temperature was 75–82°F. with a relative humidity of 30–60 per cent. Two methods were used to estimate separately the evaporative loss from the lungs and from the skin :

(i) The subject breathed into a basal metabolism machine which was placed with him on the balance. The weight loss was then due only to evaporation from the skin.

(ii) The subject was enclosed in an air-tight cylinder which was placed on the balance. He breathed through a valve to the air. The weight loss was then due only to evaporation from the lungs.

The rate of total insensible loss was slightly greater in winter than in summer, although the room temperature was kept the same.

At the environmental temperature used, it was found that evaporation from the lungs accounted for 50–60 per cent. of the total insensible loss of weight. There was no difference in weight loss between negroes and white subjects.

The rate of weight loss from corpses was rather less than the loss from the skin alone in living subjects. The authors reject the possible explanation, that some of the skin loss during life was caused by sweating. They consider that in both living and dead subjects, all the skin loss was by diffusion, but that the rate of diffusion was higher during life because of a higher skin temperature.

J. Waterlow.

WINSOR, T. & BURCH, G. E. **Differential Roles of Layers of Human Epigastric Skin on Diffusion Rate of Water.** *Arch. Intern. Med.* 1944, Dec., v. 74, No. 6, 428–36, 12 figs.

In dead skin, when the epidermis was cut away, the rate of diffusion of water through the dermis was found to be much greater than through the whole skin. In the living subject, when the superficial layers of epidermis were removed by blistering, water passed through the remaining layers much more rapidly than through intact skin. On the other hand, rate of passage through the epidermal sheet removed by blistering was the same as through normal skin. It was concluded that the barrier to free passage of water lies in the stratum corneum.

J. Waterlow.

BURCH, G. E. & WINSOR, T. **Rate of Insensible Perspiration (Diffusion of Water) locally through Living and through Dead Human Skin.** *Arch. Intern. Med.* 1944, Dec., v. 74, No. 6, 437–44, 9 figs. [10 refs.]

A method is described for measuring the rate of loss of water from the skin. A brass cup is sealed to the skin, and oxygen circulated through it. The water vapour taken up is condensed and weighed.

The rate of diffusion through dead skin was measured by suspending the skin, with a brass cup attached, in a bath of saline. When comparisons were made between living and dead skin, the temperature of the saline was adjusted to equal the skin temperature of the living subjects.

At a room temperature of 75°F. and 50 per cent. relative humidity, the rates of loss from living and dead skin were essentially the same. At 115°F. and 80 per cent. relative humidity, the rate of loss from dead skin increased only slightly, whereas from living skin it increased fourfold. The authors conclude that at the lower temperatures all the water lost from the surface of living skin had passed through the skin by diffusion. The increased rate of loss at the higher temperature was caused by sweating. Since the rate of diffusion through dead skin was not changed when the skin was kept for three or four weeks in a refrigerator, and frozen and thawed several times during that period, it is suggested that the barrier to free passage of water lies in some non-living structure. *J. Waterlow.*

MISCELLANEOUS DISEASES.

MARRIOTT, H. L. **Medical Problems of South-East Asia Command.** *Lancet.* 1945, June 2, 679–84.

This paper is packed with valuable information and suggestions, and as the author states " a comprehensive review such as this does not lend itself to summarising ". A few points from the paper follow.

Although the British and Indian troops of the S.E.A.C. are in first-class physical condition and of excellent morale there is an enormous wastage of man-days through sickness which is not of a serious nature. " One medical officer engaged in hygiene can save the work of ten medical officers in hospitals." Education of the troops is essential, and a special propaganda section would be of great value.

Malaria is the greatest problem ; it has caused half of the sickness, but its incidence is only a fraction of what it was. For security reasons it is not permissible to report in detail the measures by which this success has been gained.

The present standard treatment for British soldiers is 0·3 gm. mepacrine thrice daily for the first day ; 0·2 gm. thrice daily on the second day ; and 0·1 gm. thrice daily for five days. It is the same for Indian soldiers except that on the first day 0·2 gm. is given thrice daily.

Benign-tertian relapses are frequent, but are not of great importance.

In the treatment of cerebral malaria the Fowler position is adopted, and a nasal tube is used to maintain a constant drip into the stomach to combat dehydration.

Diarrhoea and dysentery are next in importance. Diagnosis in the past has necessarily been rough and ready ; in 20 per cent. of the cases *Entamoeba histolytica* has been found, the rest of the cases have been assumed to be bacillary, and their response to sulphonamides has been prompt in the vast majority of instances. When these drugs fail to cure within five days, a thorough investigation is carried out, and when amoebic infection is diagnosed the treatment is on standard lines. The routine treatment of all known and suspected cases of bacillary dysentery by sulphaguanidine is believed to be of great value in preventing the spread of infection.

Scrub typhus in 1944 attacked one man in every hundred exposed to risk ; the case fatality rate was 10 per cent. The patients must not be transferred

after the first few days. The essential points in treatment are : skilled nursing ; a cool ward ; maintenance of fluid and salt balance ; adequate nutrition ; and oxygen at the onset of cyanosis. Very energetic preventive measures are in train.

One outbreak of infective hepatitis was suspected of having been caused by an infected syringe used in giving cholera vaccine.

The chief causes of " heat effects " were dehydration and salt depletion. Salt should be added to the drinking water at the rate of 3 gm. per litre.

Dehydration plays an important part in every serious medical and surgical illness in the tropics : the urinary output should be measured and tested for its salt content every eight hours. A simple test is by placing ten drops of urine in a test tube, adding one drop of a 20 per cent. solution of potassium chromate, and then adding, with constant shaking and drop by drop, a 2·9 per cent. solution of silver nitrate. The number of drops needed to change the colour from yellow to brown gives the number of grammes of sodium chloride in each litre of the urine. An eight-hourly output of over 15 oz., and a salt content of 6–12 gm. per litre, are aimed at.

A sprue-like condition, occurring in both British and Indian troops, is regarded as due to malnutrition caused by the vicious circle—diarrhoea—resulting failure of absorption—deficiency of the vitamin-B complex—diarrhoea due to this deficiency. Special vitamin tablets are issued to all the troops, but these do not obviate the need for a generous diet. The treatment is directed first to the original causal factors, such as dysentery and malaria ; a high-protein, high-vitamin, and low-fat diet is given ; to this are added six compound vitamin tablets and 3 oz. marmite or similar preparation daily. Injections of liver extract, nicotinic acid (100 mgm. daily), and riboflavin (10 mgm. daily) are also given.

Anaemias are more prevalent among Indian than British troops, probably because most of the Indians elect to take milk instead of meat in their ration.

John W. D. Megaw.

PATEL, N. D. **Benign Eosinophilia with Pulmonary Shadows.** *Indian Physician.* 1945, May, v. 4, No. 5, 93–109, 3 text figs. & 8 figs. on 2 pls. [30 refs.]

An excellent account of the main features of this interesting symptom-complex about which so much has been written recently. The author's remarks are based on a study of 49 cases under his personal observation during a period of 14 months. The disease is clearly far from uncommon, if one practitioner can see so many in so short a time. Forty-seven were from Bombay Province ; 37 were males, 12 females, but since males preponderate among those seeking medical advice, this is no proof that the disease is really more common in them. The ages ranged between 8 and 56 years and the leucocyte counts up to 29,000 with 81 per cent. eosinophiles, 38,500 with 74 per cent. and 42,350 with 68 per cent. eosinophiles. No place in the aetiology could be assigned to occupation, social status, food habits, smoking or alcohol. Some who have studied this condition have emphasized the fact of there being no familial susceptibility nor other cases of allergy in the family of one affected, but the author's experience does not bear this out. Others, WEINGARTEN for example [this *Bulletin*, 1943, v. 40, 407 ; 1944, v. 41, 424], have observed that arsenic brings about complete cure and thus relapses do not occur. Dr. Patel records the case of a patient with two relapses, each after an interval of 3½ years, and a third 23 months after the second. He stresses the importance of making blood examinations and X-ray examination of the chest in all cases of chronic cough with a history of asthmatic attacks and loss of weight. He notes, as others have done, the recrudescence of the subjective symptoms and the leucocytosis and eosinophilia in the early stages of arsenical treatment, whether by injection or *per os*.

As regards the pathology and pathogenesis he thinks it is allergic and that the pulmonary interstitial tissue is sensitive rather than the bronchi (as in ordinary asthma) on the ground that the infiltration is largely in and around the alveoli. [The paper was read at a medical meeting and several took part in the subsequent discussion, but added nothing fresh, most of them relating cases in their own experience.] *H. Harold Scott.*

RANDALL, T. **Eosinophilic Pneumonitis (Loeffler's Syndrome) with Response to Emetine.** *Brit. J. Tuberculosis.* 1945, Jan., v. 39, No. 1, 37–8.

A coloured man, aged 20, was admitted to a hospital in Durban, Natal, complaining of substernal pain of one month's duration, and of severe cough with copious expectoration (occasionally blood-stained) for two weeks.

"Examination of the chest showed increased vocal fremitus and vocal resonance in the upper third of the right lung and crepitations in the right apex and mid-zone." A radiograph presented the appearances of tuberculous infiltration of both lungs "more marked on the right side, where there were several sizable areas of apparent excavitation." Eight successive examinations of the sputum showed no tubercle bacilli, nor were amoebae or fungi found. The faeces were normal. A blood examination showed: haemoglobin 14·2 gm. per cent., erythrocytes 4·3 millions per cmm., colour index 1·1, leucocytes 9,600, with neutrophiles 74 per cent., eosinophiles 6 per cent., large mononuclears 1 per cent. and lymphocytes 19 per cent.

His temperature, which had been between 99 and 100·4°F. since admission, became normal after six days in hospital, but his condition was otherwise unchanged. Emetine, 1 grain daily for 10 days, was given intramuscularly and dramatic improvement followed, all symptoms disappearing rapidly; a radiograph of the chest showed no abnormality. He was discharged cured.

The author states that there was no evidence of amoebiasis except the eosinophilia, the prevalence of amoebiasis in Durban, and the quick recovery after the course of emetine. He refers to papers by DORMER and FRIEDLANDER [this *Bulletin*, 1942, v. 39, 31] and by HOFF and HICKS [*ibid.*, 1942, v. 39, 792]. [Eosinophilia is probably not evidence of amoebiasis; see comment on DORHER and FRIEDLANDER's paper in this *Bulletin, loc. cit.*] *J. F. Corson.*

MCFARLANE, A. L. & BRANDAY, W. J. **Hepatic Enlargement with Ascites in Children.** *Brit. Med. J.* 1945, June 16, 838–40.

[Any contribution which may help to throw light on cirrhosis of the liver of obscure actiology is welcome. Many papers have been written on it, but the conclusions reached are meagre and the results show a poor return for all the work which has been done on it [see this *Bulletin*, 1938, v. 35, 909 (a careful consideration of the whole problem); 1942, v. 39, 415; 1943, v. 40, 333]. The International Commission for Geographical Pathology has made it a subject of special study (see STITT's Tropical Diseases, 6th ed., 1942, 1594, and other textbooks of Tropical Medicine).]

The authors give a brief account of 18 cases in children between one and ten years of age under their observation in a single year in Kingston, Jamaica. Two have died; the disease is usually chronic, lasting for months or even years, affects children and "ends in recovery in the majority of cases." The condition in Jamaica would seem, therefore, to differ radically from that seen in India and the Far East where the fatality rate is high and some run an acute course. The symptoms are, however, similar in many respects: early fever, anorexia, nausea, vomiting, abdominal enlargement, hepatomegaly (the liver may extend to the umbilicus and even lower), ascites, little or no jaundice. Splenic enlargement

was seen in less than half the cases. The Kahn reaction is negative (in 14 out of 15 of the authors' patients) [but a positive Kahn is of little significance in a place like Jamaica where yaws is common in children]. The blood shows "moderate anaemia" and "moderate leucocytosis." [No figures are given, which is a pity, as more elaborate laboratory procedures were carried out, such as van den Bergh reactions, sedimentation rates, fragility tests, estimations of blood urea and sugar. All but the first of these were normal.]

In the single autopsy performed the liver showed a pericellular type of cirrhosis "resembling Hanot's cirrhosis." [Histologically this is correct, but, clinically, Hanot's cirrhosis is characterized by hypertrophic cirrhosis with icterus and without ascites, whereas in the authors' cases there was ascites with little, if any, jaundice.]

The authors incline to the view that a dietary deficiency may be the primary cause, as in these patients the diet is inadequate and unbalanced, often irritant, and improvement followed change of diet alone and the same with administration of glycocoll. Dried yeast also benefited "a small number of cases."

[Since as many as 18 cases came under the authors' observation in one town in one year, opportunities should not be wanting for a deeper study of these interesting cases. Nothing is said of faecal examinations or of helminthic infestation, nor whether similar cases occur elsewhere in the island. This would seem to be a good opportunity for useful research on a subject of wide interest to the east as well as to the west.] *H. Harold Scott.*

East African Med. J. 1945, Apr. v. 22, No. 4, 126–7. **A Case of Stramonium Poisoning.**

The author of this note himself suffered from symptoms, strongly suggesting stramonium poisoning, after eating bread. The grain came from a farmer who "admitted that his farm was full of stramonium," but under the circumstances the bread could not be examined. Proof is, therefore, not conclusive [but in view of this and other reports from East Africa, it seems that the possibility should be borne in mind. The author does not say in what area the incident occurred]. *Charles Wilcocks.*

Kao, Yung-En & Chen, Shui-Chao. **A Clinical Study of Ginkgo-Nut Poisoning among Children in Kweichow. Report of 7 Cases.** *Chinese Med. J.* (Chengtu Edition). 1944, Jan., v. 62A, No. 2, 64–6.

Ginkgo nuts (*Ginkgo biloba* L.) are grown and eaten by adults in South China. For some reason, perhaps because they are known at times to cause toxic symptoms, children under ten years of age are not allowed to eat them, in Kweichow for example. The nut does not seem to be, as a rule, very poisonous, for a case is recorded of poisoning after ingestion of 1,000 of them; their toxicity would, however, appear to vary for, of the seven cases recorded here, a child aged 4 years died after eating 150, another aged 7 months died after taking seven, while others whose ages ranged from 14 months to 2 years ate from 30 to 50 and recovered. The chief symptoms are restlessness, followed by convulsions, 1–9 hours after eating the nuts, abdominal distension, dyspnoea, delayed or lost light reflexes, unequal pupils, and unconsciousness. There is usually some fever, to 40°C., with leucocytosis from 14,000 to 21,000 or more (the infant of 7 months who died had 50,000 per cmm.).

B. E. Read in a work on Chinese Foods gives the following as the composition of the nuts. The figures taken from Neil Leitch's work on *Dietetics in Warm Countries* (p. 280) are also given for comparison, since the differences are considerable. The first set are for nuts as purchased, the second are those for the edible portion.

	Protein	Fat	Carbohydrate	Crude fibre	Ash
Read ...	6·48	2·46	37·75	0·30	1·32
Leitch ...	13·4	3·0	71·2	0·5	2·8
	9·0	2·0	47·8	0·3 ..	1·9

The authors state that CHU reported in July 1943 on the chemistry and toxicology of these nuts, but say also that the actual toxic constituent is not known to them. [Work on this might be advantageously undertaken, for it is clearly a useful food (the calorie value of the edible portion is given by Leitch as 365 per 100 gm., or 2,044 per catty), but is nevertheless at times dangerous.]

H. Harold Scott.

GENERAL ENTOMOLOGY.

CHANDLER, A. C. **Factors influencing the Uneven Distribution of *Aedes aegypti* in Texas Cities.** *Amer. J. Trop. Med.* 1945, Mar., v. 25, No. 2, 145–9.

The author gives an interesting account of the spread of the ubiquitous *Aëdes aegypti* in the United States. The following is quoted from the summary.

"The prevalence of *Aedes aegypti* in early summer in Texas cities is very variable. Only in the Lower Rio Grande Valley is the winter climate mild enough to allow this mosquito to survive, without protected hold-over places, in sufficient numbers to produce a high incidence of breeding early in the season every year. In other cities early prevalence of breeding is associated with abundance of protected winter hold-over places, especially cisterns, fire-protection barrels in compresses and warehouses, or shallow wells. In cities having only a few such hold-over places, a high breeding index does not develop until late summer, and in many smaller cities such an index may not develop at all unless the mosquitoes are imported from elsewhere in automobiles or freight cars. In such cities the occurrence and prevalence of *Aedes aegypti* may vary from year to year depending on whether or not such an importation occurs early in the season. In coastal cities, alternation of cold and warm periods during the winter has a harmful effect on the survival of *Aedes aegypti*, and may be more important in holding the insect in check than the extremes of cold, or the total amount of cold weather."

R. M. Gordon.

PUBLIC HEALTH REP. Wash. 1945, Apr. 27, v. 60, No. 17, 469–70. **Use of DDT for Mosquito Control in the United States. A Joint Statement of Policy by the United States Army and the United States Public Health Service.**

The great success which has attended the use of DDT in combating insect-borne diseases during the war has fostered a hasty conclusion that it is a complete solution to all problems to which insects give rise. In this short statement, however, a warning is given that DDT, distributed over the countryside, not only destroys mosquitoes but may also kill many insects which are biologically beneficial. Much remains to be learned about the effect of DDT on the balance of nature before its general outdoor application can safely be instituted.

Extensive investigations are in hand to obtain this information, but in the meantime the joint policy of the United States Army and the United States Public Health Service is laid down in the following paragraphs :—

"1. DDT will be used for residual spray application to houses and other buildings for the purpose of killing adult mosquitoes before they have opportunity

to transmit malaria. The long-lasting killing effect of DDT as a residual spray provides a highly effective means to prevent the spread of the malarial parasite. This method of use is safe and economical, and, moreover, is welcomed by the householder because it provides freedom from insect annoyance.

" 2. The use of DDT as a mosquito larvicide will be limited to experimental investigations and to situations where DDT has definite advantage over other larvicides in saving materials and manpower, and where it presents no hazard to fish and other wildlife.

" 3. Distribution of DDT from aircraft for large-scale area control of mosquitoes in military and adjacent areas in the United States will be limited to projects conducted with due regard to the possible effects of DDT on beneficial insects and all forms of plant and animal life and in accordance with safeguards established by the Surgeons General of the Army and the United States Public Health Service."

Charles Wilcocks.

HERTIG, M. & FISHER, R. A. **Control of Sandflies with DDT.** *Bull. U.S. Army Med. Dept.* 1945, May, No. 88, 97–101, 1 fig.

Sandflies of the genus *Phlebotomus* are notoriously difficult to control but an observation of their habits suggested that they might be vulnerable to DDT films on the walls of buildings. Those species whose habits have been studied progress by short flights, alighting on stones and other obstacles as they approach a house. Instead of entering at once, they tend to alight on the outer walls and then with a series of short hopping flights, with relatively long pauses, make their way into the building. Once inside, they usually rest on the walls for some time before attempting to feed. Laboratory tests in Italy showed that contact with DDT caused a knockdown of *Phlebotomus perniciosus* and *P. parroti* var. *italicus* in 6 to 15 minutes, while *P. papatasi* required 15 to 40 minutes.

The field trials were made in the Dead Sea area, near the Jewish Agricultural Settlement. Here *P. papatasi* is abundant and cutaneous leishmaniasis is endemic. Five per cent DDT in kerosene was sprayed on to various parts of the buildings at the rate of 1 to 1·5 gallons per 1,000 square feet. The results were judged by fly counts and by statements made by the inhabitants on the number of bites. Inside spraying of the rooms gave perfect or near perfect control, with no bites reported. Spraying the outside of the openings only, and spraying the entire outside, reduced the fly counts to about a quarter and a few bites were reported. It is recommended that for practical control the entire inside walls and a part of the ceiling should be treated as well as the outside margins of windows and doors.

J. R. Busvine.

DAVIS, D. E. **The Control of Rat Fleas** (*Xenopsylla cheopis*) **by DDT.** *Pub. Health Rep.* Wash. 1945, May 4, v. 60, No. 18, 485–9.

Laboratory and field experiments were conducted to test the insecticide DDT against the tropical rat flea (*X. cheopis*), with the object of developing an additional method for the control of murine typhus. Fleas put into containers with a small amount of DDT died within a few hours, and rats were freed of fleas by dusting a small quantity of DDT into their fur. [It was noted incidentally that DDT was less effective against mites—*Liponyssus bacoti* and *Echinolaelaps echidninus*—and, surprisingly, the rat louse *Polyplax spinulosa*.] Rat-infested buildings were dusted with DDT diluted with waste flour. The powder was applied to the rat runs with a dusting gun. Rats were captured before and after dusting and examined for fleas. The average per rat from six buildings was 13·9 before and 0·6 a month afterwards. Two of these sites had an index of 0·2 and 0·5 fleas per rat four months after dusting.

A shed heavily infested with *Pulex irritans* and two garages overrun with *Ctenocephalides felis* were cleared by liberal dusting with DDT.

J. R. Busvine.

Monro, H. A. U., Briand, L. J., Delisle, R. & Smith, C. C. **Some Experiments with the Pyrethrum Aerosol under Canadian Conditions.** *74th Rep. ent. Soc. Ont. 1943.* Toronto. 1944, 42–5. [Summary taken from *Rev. Applied Entom.* Ser. B. 1945, May, v. 33, Pt. 5, 73.]

The results are given of experiments in Canada in 1943 on the control of insects with an aerosol consisting of 5 per cent. pyrethrum extract containing 20 per cent. pyrethrins, 2 per cent. sesame oil and 93 per cent. dichlordifluoromethane. It was usually dispersed from a five-pound storage cylinder through a steel capillary tube 5 inches long with an internal diameter of 0·017 inches, soldered on an oil-burner nozzle. The nozzle was intended only to hold the tube, but its wire filter helped to prevent clogging. Hypodermic needles of various internal diameters and lengths mounted directly on to the cylinders were also used with success.

Simuliids readily entered a sail silk tent at an experiment station in New Brunswick when the weather was fair and warm. At 75°F., the aerosol applied with the capillary tube at 0·05 oz. per 1,000 cu. ft. caused 50 per cent. of the Simuliids to drop and at 0·1 oz. it caused them all to drop in 1–3 minutes. All those that dropped at either rate of application died within eight hours. Up to 0·25 oz. was required at about 60°F. In experiments in Quebec, exposure to 0·1 oz. per 1,000 cu. ft. for one hour at 70–80°F. caused complete mortality of all flies tested, which comprised Simuliids, Tabanids, Muscids, Sarcophagids and Calliphorids. Aerosols are generally unsuitable for use against *Blattella germanica*, L., because many of the cockroaches are driven away by the stimulating action of the pyrethrum and eggs are not killed. However, in dining cars on trains, where the use of powders might be dangerous, the active population of *B. germanica* was reduced by 90–95 per cent. at temperatures above 60°F. by one application of the aerosol at the rate of 2 oz. per 1,000 cu. ft., using the capillary tube. The whole car was treated after the kitchen and pantry at the first application to kill escaping cockroaches or those free in the body of the car. Only the kitchen and pantry received the subsequent applications, of which as many as seven were made at intervals of 1–4 weeks. This treatment reduced the population to what appeared to be an irreducible minimum. When using the aerosol at this dosage, it was advisable to wear a respirator equipped with a filter used against particulate suspensions.

Chang, K. **Domestic Flies as Mechanical Carriers of certain Human Intestinal Parasites in Chengtu.** Reprinted from *J. West China Border Research Soc.* 1943, v. 14, Ser. B., 92–8.

The author has attempted to assess the importance of various flies as carriers of human intestinal parasites, by examining the contents of their intestines removed by dissection, or centrifuged suspensions of their faeces, or centrifuged suspensions of ground-up flies. In these three ways 3,076 domestic flies caught in Chengtu were examined, the species being *Musca vicina*, *M. sorbens*, *Chrysomyia megacephala*, *Lucilia sericata*, *L. caesar*, *Sarcophaga* spp., *Aldrichiella grahami* and some unidentified flies.

By the first method, 15·6 per cent. of 423 flies were found positive, the parasites including *Entamoeba histolytica* cysts and cysts of other protozoa, and ova of *Ascaris*, *Trichuris* and hook-worms. The flies which carried human intestinal parasites were *C. megacephala*, *L. sericata* and *Sarcophaga* spp., but not one of the house flies, *M. vicina*, was positive. The findings obtained by the other two methods did not give results so interesting as those found by the first.

The author comments that these findings correspond with the habits of the flies. *Musca vicina* prefers cooked food to faeces and garbage, and is known as

the rice fly. It breeds in pig manure, unlike *C. megacephala*, which breeds in liquid human faeces and haunts insanitary latrines, of which there are many thousands in Chengtu. It seems that flies may transmit *Ascaris* and *Trichuris*, but these, being transmitted much more efficiently by other means, are probably not important in this connexion ; in the transmission of *E. histolytica* and its associated protozoa, however flies may play an important part.

Charles Wilcocks.

VANDERPLANK, F. L. **Apparent Densities of certain African Blood-Sucking Insects (Diptera).** *Proc. Roy. Ent. Soc. London.* 1944, v. 19, Pt. 4–6, 68–72. [Summary taken from *Rev. Applied Entom.* Ser. B. 1945, May, v. 33, Pt. 5, 83.]

Tabanids and *Glossina* spp. were collected on 1–11 days in each month from November 1940 to August 1941 on a tethered ox in a hardpan area near Old Shinyanga in Tanganyika Territory. The ox was being used for attracting *Glossina*. Tables show total monthly catches and mean monthly catches for a specified period of both sexes of *Glossina swynnertoni*, Aust., and *G. pallidipes*, Aust., and of females of *Nuceria neavei*, Aust., three species of *Tabanus*, two of *Pangonius*, three of *Dorcaloemus*, and unidentified species of *Haematopota*. Data are also given on the monthly rainfall and mean maximum and minimum screen temperatures. The catching site and methods used are described. *Tabanus* and *Haematopota* were caught in most rainy months, but *Pangonius*, *Nuceria* and *Dorcaloemus* only during April and May, towards the end of the rains. *G. pallidipes* decreased in numbers from November to December and then gradually increased. *G. swynnertoni* increased during the rains and decreased during the dry season. *Tabanus* was active towards mid-day, when *Haematopota* was inactive except on cloudy days. *Pangonius* was most active at mid-day and during the afternoon. *P. zonatus*, Wlk., was taken in extremely large numbers during April, and it is suggested that it may be a factor contributing to the high incidence of trypanosomes in game at that period.

BISHOPP, F. C. & TREMBLEY, Helen L. **Distribution and Hosts of certain North American Ticks.** *J. Parasitology.* 1945, Feb., v. 31, No. 1, 1–54, 18 figs. [Numerous refs.]

In this paper the distribution of some 31 species of North American ticks is mapped from records compiled at the Bureau of Entomology and Plant Quarantine. Full lists are given of the hosts and the numbers of ticks of each stage collected from them. This throws an interesting light on the question of host specificity, for although the host list for each species is often extensive, relatively few appear to serve as major hosts.

Notes are also included on seasonal activity, the site of attachment to the host and the medical importance of the ticks. The latter summarizes what is known of each species as a disease carrier. Apart from this, however, the willingness of certain species to attach to man may constitute a source of considerable annoyance.

A. D. Lees.

MISCELLANEOUS.

COLONIAL OFFICE. **Report of the West Indian Conference held in Barbados 21st–30th March, 1944** [STOCKDALE, F., Chairman]. Colonial No. 187. pp. vi+21. 1944. London : H.M. Stationery Office. [6*d.*]

The Conference was held in Barbados from March 21st to 30th, 1944, and the Report is dated March 30th, 1944. It comprised representatives of the following

local Governments :—Bahamas, Barbados, British Guiana, British Honduras, Jamaica, Leeward Island, Porto Rico, Trinidad, Virgin Islands of the United States, and Windward Islands, together with representatives of the Anglo-American Caribbean Commission (with United States and British Sections) and its advisory body, the Caribbean Research Council.

In the Introduction, a short history of the development of the Conference is given ; in 1943 the British and United States Governments agreed to collaborate for the improvement of social and economic conditions in the Caribbean area, and established the Anglo-American Caribbean Commission ; more recently, the Caribbean Research Council was formed as an advisory body to the Commission for the co-ordination of scientific and technical work.

The next step was to provide for consultations with local representatives, official and non-official, of the territories concerned, by establishing a series of West Indian Conferences " under the auspices of the Anglo-American Caribbean Commission." The Conference will be a standing body with a central secretariat, and will meet from time to time to consider special subjects. Each British or United States territory may send two delegates accompanied by advisers. The Conference will be purely advisory and have no executive powers unless such are specially entrusted to it by Governments. Other countries may be invited to participate on occasions.

While recognizing the existence of many other problems which will require and receive attention, it was decided at this first session of the Conference to restrict discussion to the following subjects : 1.—Means for raising the nutritional level ((*a*) local food production, (*b*) expansion of fisheries) ; 2.—Re-absorption into civil life of persons engaged in war employment ; 3.—Planning of public works for the improvement of agriculture, education, housing, and public health ; 4.—Health protection and quarantine ; 5.—Industrial development ; 6.—The Caribbean Research Council—possibilities for expansion.

Committees were appointed to consider and report on these items and their reports, of which there are seven, form the main contents of the present Conference Report.

I. Item 1(*a*).—Greater local production and use of protective foods—meat, milk and dairy products, legumes, eggs, fruit, and leafy vegetables—is required. It " must depend largely upon remunerative returns from the export of staple crops."

Considerable improvement in the conditions of rural living is needed, *viz.*, increased income, better water supply, light and power, education and medicine, housing, etc.

The Committee made detailed recommendations, some of which refer to action by the Governments concerned and include the acquirement of land, provision of suitable conditions of land tenure by small settlers, processing and storage of food, provision of assured food markets at suitable prices, agricultural credit agencies, purchase and sale of basic foodstuffs by Government, supply of seeds, implements and livestock, educational food propaganda, provision of milk for infants and lunches for school children ; food research must be intensified.

II. Item 1(*b*).—The fishing industry should be expanded ; the means will vary in different territories. Among subjects to be considered for development are shark, crawfish and shrimp fishing, freshwater fishing, sport fishing and the tourist trade, marketing and distributing, price control, welfare measures among the fishing population. The need for research on methods of capture, handling and preservation of fish, as well as fundamental research, is strongly urged. The Committee gave a list of recommendations, including the continued support of the Anglo-American Caribbean Commission.

III. Item 2.—The Committee recommended that members of the Services should be allowed to remain in the Services for at least six months after

demobilization, and be given vocational training and assistance in finding employment. They should be given preference over other candidates by official and private employers, and representative committees should be appointed to study, arrange and supervise this.

IV. Item 3.—It was strongly recommended that public works construction should be undertaken to relieve unemployment so far as it could be done without interfering with the war effort ; long-term plans should be made. Legislation to control land and prevent improper exploitation should be prepared. Regional Planning Boards should be appointed and a Caribbean Planning Commission should form part of the Anglo-American Caribbean Commission for the co-ordination of regional planning. The subject is treated in some detail.

V. Item 4.—A. Quarantine. The main recommendations of the British West Indian Quarantine Conference, held at Trinidad in November 1943, should be carried out.

B. *Tuberculosis.* The usual general measures for raising the standard of living are referred to ; as special measures the Committee recommended the provision of clinics with X-ray apparatus, of tuberculosis hospitals and sanatoria, and provision for rehabilitation. Co-ordination on a regional basis will be required.

C. *Venereal Disease Control.* The need for control is urgent ; the usual measures were recommended.

D. *Sanitation.* Improved sanitation was regarded as urgently needed.

E. Nutrition. A scientific investigation has been approved and awaits the release of a research officer ; the Committee urged that all steps to expedite the investigation should be taken.

VI. Item 5. The establishment of self-supporting new industries and the expansion of existing ones were strongly recommended, but not industries that would require a continued subsidy. Predatory " dumping " by Great Britain or the United States should not be allowed and these countries should be asked to prevent it. Local Governments should give all facilities for the development of industries.

VII. Item 6. The Caribbean Research Council already has Sectional Committees on Agriculture, Nutrition, Fisheries and Forestry ; it was recommended that the following should be added : Public Health and Medicine ; Industries ; Building and Engineering Research ; Social Sciences.

The Conference adopted the various recommendations and called for prompt action by the various Governments concerned. To promote the expansion of trade within the area, the abolition of import duties on foodstuffs produced within the area should be considered.

The Anglo-American Caribbean Commission was asked to establish a permanent secretariat to deal with the work of the West Indian Conferences.

J. F. Corson.

Africa Méd. Lisbon. 1945, Feb., v. 11, No. 2, 39–70. Reforma dos Serviços de Saúde do Império Colonial Português. [**The Reform of the Health Services in the Portuguese Colonies.**]

In this paper is reproduced the text of decree 34,417 of the Minister for the Colonies, dated February 21st 1945, which deals, in 159 Articles, with the reorganization of the colonial health services.

Manson-Bahr, P. **Co-operation in the War against Disease.** *Nature.* 1945, May 19, 593–6.

In this article the author re-states the principal known facts concerning the transmission and spread of certain major tropical diseases, and comments

briefly on other conditions of great importance in hot climates, including the state of nutrition of the people. These facts lead to the conclusion that it is essential, in the control of these transmissible diseases, that all governments should combine in some form of international organization, one of whose duties should be to ensure that an outbreak of disease in one country is immediately made known to all others. In recent years there have been several organizations, but each has been incomplete. Moreover, each country should produce annually a report on the public health of the previous year, which should be freely and easily accessible to all other governments, as are the reports of Britain and the Colonies, and of some other countries. This service is far from complete throughout the world.

Knowledge of advances in medical science is spread through the medium of an enormous number of medical journals, in many languages, and medical men cannot hope themselves to read so great a mass of literature. [It is and has been the function of the Bureau of Hygiene and Tropical Diseases to collect and abstract the medical literature of subjects with which it deals, so that this difficulty may be overcome.]

The author also touches upon the subject of medical education of tropical populations, and on the duties of the more advanced to the less advanced races.

Charles Wilcocks.

BOOK REVIEWS.

HEADLEE, Thomas J. **The Mosquitoes of New Jersey and their Control.** pp. x+326, 84 figs. 1945. New Brunswick: Rutgers University Press. [$4.00.]

The history of the New Jersey Mosquito Extermination Association extends back to the year 1900, when Dr. J. B. SMITH secured from the New Jersey Agricultural Experimental Station a small sum of money to enable him to undertake a preliminary investigation of the local mosquito problem. From this small beginning was created a great and important scientific institute with many branches, of which the publications are known to all who are interested in the study of mosquito control.

Dr. HEADLEE, who succeeded Dr. SMITH and who has served on the staff of the Association for more than thirty years, has now applied his unique knowledge and ripe wisdom to the task of recording the eventful history of this forty-five years' war on the New Jersey mosquitoes. He recounts how, until 1899, the mosquito bred unchecked in New Jersey and that "Salt-marsh-bred species migrated for long distances over the upland, reaching points more than thirty miles away in large numbers and infesting seriously more than one-half the state's land surface and annoying very seriously nearly three-fourths of the population." He tells how, in 1900, war was declared on the insect horde by a small but determined group of investigators, how they studied the habits and breeding places of the insect enemy, and how, as the knowledge which they acquired enabled them to clear small areas of mosquitoes, other citizens (doctors, public health officials, engineers and legislators) ceased to be sceptical and joined with the entomologists, so that the movement grew apace. From that time onwards the history is one of almost constant successes achieved in the face of great difficulties, though the author does not hesitate to record the few temporary reverses.

Dr. Headlee shows that the victories which resulted in reducing the mosquito incidence in New Jersey depended on the studies previously made of the life histories and habits of the local mosquitoes. Thirty-one species are considered in the book and the bionomics of each of these species, together with the methods to be employed for recognizing their larval and adult stages, are discussed in detail and occupy nearly two-thirds of the volume. In the space remaining at his disposal, Dr. Headlee gives an account of how the knowledge gained from these studies has been utilized to devise anti-mosquito measures against both larvae and adults, and adds an account of the laws which have been enacted to give force to these measures. The first of these was passed in 1902 and reads :

> " BE IT ENACTED by the Senate and General Assembly of the State of New Jersey :
>
> 1. The New Jersey Agricultural Experiment Station be and the same is hereby empowered and directed to investigate and report upon the mosquitoes occurring within the state, their habits, life history, breeding places, relation to malarial, and other diseases, the injury caused by them to the agricultural, sanitary, and other interests of the state, their natural enemies, and the best methods of lessening, controlling or otherwise diminishing the numbers, injury or detrimental effect upon the agricultural, sanitary, and other interests of the state."

This is indeed an enlightened document when compared with the difficulties encountered by Ross in his campaign in the British Empire.

The book concludes with an interesting chapter on the economic effect of mosquito reduction, which shows the annual tax-value increase in areas in New Jersey with and without progressive mosquito control. These figures of financial improvements are very convincing and the reviewer wonders whether similar figures could not be made available in Britain to show the remarkable effects which have followed Mr. Marshall's successful work on Hayling Island.

The systematist will find this book of only local interest, but those who are interested in the history of entomological research and its practical application to human problems will find much fascinating reading, and from a study of its pages can forge a trustworthy weapon to defend the view that entomological research is the concern of the state as well as of the individual.

R. M. Gordon.

Treston, M. L. [C.B.E., F.R.C.S., F.R.C.O.G., I.M.S., Inspector-General of Civil Hospitals, Burma]. **Health Notes for Government Officials.** 64 pp., with Appendices, 8 folding plans & 3 figs. Published by the Director of Public Relations, Government of Burma. [n.d. ; n.p.]

During the present century there have been many medical men who have turned their attention to the exposition of medical knowledge for the benefit and instruction of the public. This is a tendency to be encouraged, since the argument in favour of popular understanding of the basic facts of certain diseases (especially the transmissible diseases and the deficiency states) is very strong, but the technique of presentation needs careful thought and study. Too often, booklets of this kind give the impression of uncritical haste in the writing and of an insufficiently considered plan of presentation ; the result, usually, is a series of brief chapters of dogmatic statements, without sufficient explanatory matter to create in the mind of a non-medical reader a satisfactory grasp of the elements of disease causation and transmission. To the reviewer it seems that any book of this kind which fails to explain the nature and effects of bacteria, protozoa and other parasites must largely fail in its object.

The small book by Colonel Treston is not an exception in this respect. Two examples may be taken to illustrate the point. On page 3 the remark is made :

" Have anyone who handles food or utensils, *tested* to make sure that he is not a carrier," but up to that point no explanation has been given as to what a carrier is, or what, in this connexion, he may be carrying. Later, the malaria parasite is mentioned, but not explained or described. Other instances can be found.

This is not the only criticism which may be made against the book. There are inaccuracies which can hardly be excused. For instance: "Infection with worms is nearly always through an abrasion in the skin" (p. 15), shop typhus is transmitted " by the bed bug, the flea and the tick " (p. 23); fleas " have a jumping range of 2 feet and carry two stings, the ' one in the tail ' transmits plague, typhus and relapsing fever " (p. 32); bugs " are credited with carrying Typhus and Kala Azar " (p. 34). The advice given on page 7, that " one tablet of Mepacrine Hydrochloride (Atabrin) 0·1 grm., i.e. 1½ grains twice weekly, on two successive nights, is of value " in prevention of attacks of malaria conflicts with general experience and with the careful work done by FAIRLEY [this *Bulletin*, 1945, v. 42, 656]; such small dosage can hardly be useful in suppression, and may lead to trouble by giving a false sense of security or by masking the disease.

These criticisms are valid, but that does not mean that much of the advice given is not correct. Nevertheless, it seems to the reviewer that those who write books of this kind should consider very deeply the methods they adopt of presenting the subject to non-medical readers, and that they should be at pains to ensure accuracy.

The author has included plans for layout of a small town, for the construction of a well, a bored-hole latrine and a slaughterhouse, and a table of daily food requirements calculated for Burmans. *Charles Wilcocks.*

MEDICAL CLINICS OF NORTH AMERICA. 1944, Philadelphia Number, 1293–553, numerous figs. & charts. **Symposium on Recent Advances in Medicine.** [Reprinted by the U.S. Office of War Information from the *Med. Clinics of North America* for November, 1944.]

This symposium is reprinted by the United States Office of War Information from *The Medical Clinics of North America* for November, 1944, no doubt because the authorities recognize the value of brief papers which bring together the important new facts of medicine, for those readers who have neither the leisure nor the opportunity themselves to read all the relevant literature as it appears in the medical journals. This function is well performed in the Symposium. The first half deals with recent work on Air Sanitation, Otolaryngology, Cardiovascular Disease, Gastro-enterology, Thyrotoxicosis, Leukaemia, Pituitary Myxoedema, Rabies, Acute Respiratory Infections, and Fluorine. The second half, from the Pennsylvania Hospital Overseas, is concerned with certain subjects more allied to the contents of this *Bulletin*. A general account of immunity, pathology and clinical manifestations in malaria is given by VANDER VEER and HEDBLOM, which is useful in that it stresses the importance of malaria in tropical warfare, and the need to be constantly watchful for pernicious symptoms. Laboratory diagnosis in malaria is summed up by DENHOFF. The clinical aspects of scrub typhus are dealt with, in the form of a comment on a case, by DUNCAN, and there is a fairly full account of dengue by EWING. MCCLENAHAN gives a short account of leprosy and its relation to soldiers mixing with a population in which it is endemic, and HAINES and FORCEY an account of 40 cases of primary atypical pneumonia in troops in the South Pacific. The dysenteries are briefly discussed by CALARCO.

The remaining papers are concerned with Anxiety Neuroses, Fractional Gastric Analysis, and Thyroid Disease, but there is also a useful paper on the

treatment of common skin diseases in the tropics—epidermophytosis, dermatitis venenata, and bites by insects and mites, which deserves attention.

The publication is well produced and printed. *Charles Wilcocks.*

HUNT, Virginia Lloyd. **How to Live in the Tropics.** pp. ix+178. 1942. New York: Harcourt, Brace & Company. [12s. 6d.]

This useful book, written for non-medical persons, contains chapters on Preparations, Climate, Environment, Daily Routine, Food and Drink, Hobbies, Women and Children, Insects, Communicable Diseases, Home Nursing and First Aid. It is attractively written and the advice given is sound. It can be recommended to intending travellers to the tropics. *Charles Wilcocks.*

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